The *over-simplification* of inhibitory control in heavy drinkers: investigating individual differences in proactive and reactive control, the response to environmental and psychological triggers, and the predictive utility for alcohol use.

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy by Laura Baines (October, 2019).

Table of Contents

List of tables

List of figures

Inhibitory control and alcohol use: a more complex understanding.

Laura Baines

Abstract

Poor inhibitory control is thought to play a key role in Alcohol Use Disorders. However, there is an *over-simplistic* conceptualisation of inhibitory control as a reactive stopping response in the literature. This thesis aimed to investigate the relationship between 'reactive' and 'proactive' inhibitory control and alcohol use in non-dependent, heavy drinkers. Specifically, to investigate whether exposure to environmental and psychological triggers (alcohol intoxication, alcohol-cue exposure and exposure to acute stress) lead to short-term impairments in reactive and proactive control, and whether these impairments were related to increased alcohol-seeking. Lastly, this thesis aimed to explore potential mechanisms which may underlie these relationships. These theories are discussed in detail in chapter one, and the general methods used throughout the experimental studies in this thesis are described in chapter two.

In chapter three, both reactive and proactive control were isolated in heavy drinkers during inhibitory control tasks, however, there was no association between individual differences in proactive or reactive control and individual differences in alcohol use. Chapter four then sought to investigate if impairments in inhibitory processes (reactive control, signal detection and proactive slowing) fluctuated in response to alcohol-cue exposure (study two) and alcohol-intoxication (study three). The results demonstrated that alcohol-cue exposure and alcohol intoxication increased *ad libitum* alcohol consumption, but this was unlikely due to impairments in inhibitory processes.

In chapter five, two online studies demonstrated that individual differences in proactive slowing and reactive control were unrelated to individual differences in alcohol consumption. I also found limited evidence for mechanisms (Working Memory Capacity, alcohol sensitivity) which may underlie effective use of proactive control. Finally, chapter six sought to provide both behavioural and neurophysiological evidence to investigate whether acute stress impaired inhibitory control processes, in the presence of alcohol-related cues.

The results demonstrated that acute stress had limited effects on reactive stopping, and no effect on proactive inhibitory processes or the neurophysiological responses of inhibitory control. In contrast, alcohol-cue exposure impaired proactive stopping and increased P300 responses (compared to neutral-cues). However, there was little evidence of a relationship between inhibitory processes (or neurophysiological responses) and alcohol consumption, or for the suggestion that Working Memory Capacity or alcohol sensitivity may underlie the effective use of proactive control.

The overall results of this thesis suggest that inhibitory control is a multi-component process that is comprised of both reactive and proactive control. Specifically, there was limited evidence that impairments in these processes fluctuate in response to psychological and environmental triggers. Certainly, this thesis failed to find a consistent relationship between both reactive and proactive inhibitory processes and alcohol use, contradicting theories that posit inhibitory control as a key mechanism for substance addiction.

Dissemination

I submit this thesis in partial fulfilment of the conditions for a PhD by published papers. The experimental chapters (chapter three to chapter six) take the form of journal article manuscripts in accordance with the guidelines for the University of Liverpool. These have either been published before submission (chapter three, chapter four), are under review in a peer-reviewed journal (chapter five), or are prepared for publication (chapter six). As required, specific details of each article submission (including the contribution of authors) are given at the beginning of each chapter.

Declaration

This thesis is the result of my own work. No portion of this has been submitted either wholly or partly in support of any other degree or qualification at this or any other University.

Acknowledgements

A huge thank you to Andrew Jones for giving me the opportunity to study for this PhD and who has been a fantastic, supportive supervisor throughout the whole four years. I'd also like to thank Paul Christiansen and Matt Field, who have provided me with excellent feedback on the manuscripts in this thesis to improve the clarity of my writing. Special thanks to my mum and dad for all their love and support, and who have enabled me to pursue higher education, and of course to Liam for his unconditional support and encouragement. Without these people, along with my other close family and friends who have helped me through difficult circumstances in relation to my dad's illness, completion of this thesis would not have been possible. Lastly, I'd like to thank the friends (particularly fellow demonstrators) I have made in the department for all their supportive chats and coffees, as well as the participants who took part in my research.

This thesis is dedicated to my dad, Jimmy Baines, who I know would be so proud of me for completing this PhD.

Chapter 1

General Introduction

1.1 Alcohol use statistics

Hazardous alcohol consumption is a global risk factor for population health *(Global Status Report on Alcohol and Health, 2018)*. The latest report by the World Health Organisation (WHO) suggests that 2.3 billion people drink alcohol around the world. Certainly, alcohol plays a central role in various social occasions and religions, whilst also having medicinal purposes in many countries (Hanson, 2013). Specifically in the UK, a recent government survey reported that 58% of individuals aged over 16 had consumed alcohol in the preceding week, which is equal to 25.6 million adults in England. Importantly, although the majority of these adults may not consume alcohol continually at high-risk levels, or indeed be alcohol dependent, there is a range of unsafe drinking patterns in the UK and the rest of the world. This covers both occasional hazardous (or binge) drinking, and more frequent daily heavy drinking, all of which produce significant public health concerns (*Statistics on Alcohol, England*, 2018). Consequently, in the UK there are government guidelines and restrictions in place to try and reduce the number and severity of negative consequences experienced by individuals, and wider society as a result of alcohol misuse.

1.2 UK Government guidelines

The Chief Medical Officers' guidelines recommend that men and women should not drink more than 14 units of alcohol per week, in order to reduce potential health risks from drinking. These units should also be consumed over at least 3 days to reduce the possibility of death from accidents, injuries and sickness. Those who drink excessively or too fast in one session, as well as those who drink more than the recommended units, can put themselves at increased risk of injury or death, a loss of self-control and a miscalculation of hazardous circumstances. Despite this, government statistics reported that in 2016, approximately 11.4 litres of pure alcohol were consumed per adult (over the age of 15) in the UK that year (Global Status Report on Alcohol and Health, 2018). As 10ml of pure alcohol corresponds to one UK unit, this is the equivalent of 22 units per week (e.g. approximately 8 pints of beer (5.0% ABV) or 11 medium (175 ml) glasses of wine (12% ABV)), which is above the

suggested recommendations. Furthermore, a report by Public Health England (*Local Alcohol Profiles for England: March 2017*, 2017) demonstrated that 25.7% of adults in England frequently consumed more than the recommended 14 units per week between 2011-2014, with 16.5% of adults binge drinking on their heaviest drinking day. Therefore, many individuals in the UK are putting themselves at risk of alcohol-related harm. Certainly, there are extensive health and socioeconomic consequences of alcohol misuse and dependency, not only to the individual but also to the wider community.

1.3 Alcohol-related consequences

1.3.1 Health consequences

Firstly, alcohol consumption has been recognised as a contributing factor to at least 200 health conditions such as heart disease, various cancers and strokes (Rosenberg et al., 2017). The latest report from the WHO (*Global Status Report on Alcohol and Health*, 2018) suggests that in 2016, 3 million global fatalities and 132.6 million disability-adjusted life years were the product of alcohol-related harm. That is approximately 5.3% of global deaths with various alcohol-related causes, such as injuries (28.7%), diseases (digestive 21.3%, cardiovascular 19%, infectious 12.9%) and different types of cancers (12.6%). Consequently, only smoking and obesity are bigger risk factors for mortality and/or disability. Specifically in the UK, there were 5,507 deaths due to alcohol-related harms in 2016 and 337, 000 alcohol-related hospital admissions in 2016/2017 (*Statistics on Alcohol, England*, 2018). Consequently, the National Health Service (NHS) annually incurs approximately £3.5 billion of costs linked to alcohol (*Local Health and Care Planning: Menu of preventative interventions*, 2016).

Furthermore, it is often the case that co-morbidity of Substance Use Disorders and mental health problems occur. According to government statistics published in 2016 (*Health Matters: Harmful Drinking and Alcohol Dependence*, 2016), hazardous drinking or drug use was reported in 44% of community mental health patients in the previous 12 months. Suicidal behaviour is also a frequent issue amongst those with a diagnosis of alcohol dependence (Wojnar et al., 2009). For example, in 45% of mental health patient suicides between 2003-2013 there was an history of hazardous drinking (*National Confidential Inquiry into Suicide and Homicide by People with Mental Illness*, 2015). Therefore, it is essential to try and pinpoint contributing factors to alcohol misuse and dependency, not only to protect individuals but also to reduce the burden of alcohol-related costs on the NHS.

1.3.2 Socioeconomic consequences and crime

Alcohol misuse is also related to further significant financial and social costs to society, despite increasing in affordability by 64% in the UK since 1980 (*Statistics on Alcohol, England*, 2018). Government statistics suggest that £7 billion in productivity is lost through alcohol use, due to illness and unemployment annually, with a seemingly reciprocal relationship between unemployment and alcohol consumption (Boden, Lee, Horwood, Grest, & McLeod, 2017). Indeed, Substance Use Disorders are suggested to be both a cause and consequence of financial stress (Compton, Gfroerer, Conway, & Finger, 2014).

Alcohol is also suggested to be involved in approximately half of all violent offences and 360,000 domestic violence cases in the UK, with £11 billion lost to crime involving alcohol in the UK annually (*Alcohol units - A brief guide*, 2008). Specifically, a UK government crime survey (*Crime survey for England and Wales*, 2013-14) reported that in 53% of violent crimes in England and Wales, victims believed the offender(s) had consumed alcohol. This equates to 704,000 violent cases. In addition, 64% of violent incidents that occurred between strangers were alcohol-related, with increasingly severe injuries in these cases compared to non-alcohol related incidents. Thus, it is clear that alcohol misuse plays a substantial role in socioeconomical costs and crime statistics.

1.4 Alcohol Use Disorder

The statistics reported so far emphasise the issues associated with harmful drinking in the UK and the rest of the world. Regular heavy drinking (>14 units per week) is also suggested to increase the risk of developing alcohol dependence, with 80, 000 individuals receiving treatment for problematic alcohol use in 2016/17 in England (*Statistics on Alcohol, England*, 2017). In the most recent Diagnostic and Statistical Manual of Mental Disorders (DSM-5), there were significant modifications to the diagnosis of substance (alcohol) dependence (Reichenberg, 2013). The manual has now combined the separate categories of alcohol abuse and dependence into one specific disorder; Alcohol Use Disorder. This ranges from mild to severe and requires two symptoms (from the following 11) to be met in the previous 12 months in order for a diagnosis to be made. The list of 11 symptoms include:

1) "Drinks more than intended, or for longer than intended
2) Efforts to control or cut back on drinking have been unsuccessful
3) Large amounts of time are spent obtaining, using or recovering from alcohol
4) Cravings (the presence of a strong desire to drink)

5) Recurrent use resulting in problems at work, home or school
6) Continued use despite recurrent social or interpersonal problems resulting from drinking
7) Curtailing important activities in favour of alcohol use
8) Alcohol use despite potentially hazardous outcomes (drinking and driving, for example)
9) Continued alcohol use despite knowledge that alcohol use is causing or exacerbating a persistent physical or psychological problem
10) Tolerance or a need for increased amounts of alcohol
11) Withdrawal symptoms"

Furthermore, the severity of diagnosis is based upon the number of symptoms met:

- "Mild: presence of two to three symptoms
- Moderate: presence of four to five symptoms
- Severe: presence of six or more symptoms"

As discussed, regular heavy drinking (>14 units per week) is suggested to put individuals at increasingly higher risk of many health-related, socioeconomic and other negative consequences. Therefore, the importance of pinpointing factors that may contribute to heavy drinking and the possible development to alcohol dependence cannot be underestimated. The identification of these contributing factors may allow valuable interventions to prevent recreational alcohol use from developing into harmful levels and dependence. This could have positive results for both the individual user and wider society, particularly reducing the burden on the NHS from alcohol-related costs. Therefore, to allow an investigation of factors which may contribute to the transition from heavy drinking to dependence, the research presented in this thesis aimed to recruit individuals who were consuming more than 14 units per week (i.e. heavy drinkers), but who had not received a previous or current diagnosis of alcohol dependence.

1.5 Reduced self-control

Contemporary models of addiction suggest that substance addiction is either a brain disease or the product of deep-learning (Lewis, 2017; Volkow, Koob, & McLellan, 2016). The most influential of these describe substance addiction through a combination of biological processes, social processes (e.g. behavioural models), and/or psychosocial processes (e.g.

environmental factors) (Teesson, Hall, Proudfoot, & Degenhardt, 2012; West, 2001). However, there is no single widely accepted theory as of yet which acknowledges all of these viewpoints/processes.

Nevertheless, there are some overlapping similarities in models of addiction. Most prominently, across these theories an impairment in self-control has been regarded as central to substance abuse (Fillmore, 2003). That is, when an individual loses control over drug seeking and consumption (Everitt, 2014). Indeed, this 'loss of control' over behaviour (often also referred to as impaired or reduced control) is viewed as a crucial factor for substance addiction (Fillmore, 2003), and is regarded as a key diagnostic criteria for Alcohol Use Disorder. As such, a 'loss of control' is consistent with at least the second DSM-5 criteria for Alcohol Use Disorder described above (i.e. "*Efforts to control or cut back on drinking have been unsuccessful*"), however it overlaps with other criteria too (e.g. *"Drinks more than intended, or for longer than intended").* Consequently, various explanations of substance addiction recognise this 'loss of control' in reward-driven substance seeking behaviour.

1.6 Inhibitory control

1.6.1 Definition

Inhibitory control (or disinhibition) is defined as the (in)ability to suppress, postpone or alter a response that is no longer necessary (Logan, Cowan, & Davis, 1984), and therefore shares significant overlap with a 'loss of control' and self-regulation (Baumeister, 2014). Specifically, Baumeister et al (Baumeister, Heatherton, & Tice, 1994) suggest that 80-90% of self-regulation behaviour requires the inhibition of a response. Indeed, without the ability to monitor and regulate behaviour, individuals would be incapable of inhibiting and changing their behaviour when necessary and instead, would instantly react to the stimuli that motivates them most in their surroundings (Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014). In the context of substance addiction, this could include a failure to resist cravings (Baumeister, 2014). As a result, poor inhibitory control has been implicated in the development and continuation of substance misuse (e.g. (de Wit, 2009; Fillmore, 2003; Goldstein & Volkow, 2002; Yucel et al., 2019)), gambling (Billieux et al., 2012; Brevers et al., 2012; Goudriaan, Oosterlaan, de Beurs, & van den Brink, 2006), obesity (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006; Spitoni et al., 2017), as well as various psychological disorders such as Obsessive-

Compulsive Disorder (OCD) and Attention Deficit Hyperactivity Disorder (ADHD: (Murphy, 2002; Norman et al., 2019; van Velzen, Vriend, de Wit, & van den Heuvel, 2014)).

Focusing on substance addiction, there are numerous theories which posit impairments in inhibitory control as a candidate psychological mechanism. For example, de Wit (de Wit, 2009) argues that dimensions of impulsivity (including inhibitory control) are both a cause and consequence of substance use. Specifically, that trait impulsivity is a risk factor for developing a Substance Use Disorder and failing to abstain in those already with an addiction. Furthermore, components of impulsivity (including inhibitory control) are also suggested to fluctuate *within* individuals, and these fluctuations may increase substance use, which can be particularly problematic in those trying to abstain. In contrast, the consequences of both acute and chronic substance use may also lead to increasingly impulsive behaviour, which then may promote further substance use or misuse.

As a second example, Everrit et al (Everitt et al., 2008) also recognise 'a loss of control' in their model of drug addiction, which describes the transition from voluntary substance use to uncontrollable, habitual use. However, they also specify that this transition reflects a shift in neural transmission from the pre-frontal cortex to striatal control over substance use behaviour. Contrastingly, other theories focus on impairments in inhibitory control in combination with the hyper-valuation of substance cues which result in increased substance use or relapse (Volkow, Wang, Tomasi, & Baler, 2013). For example, Goldstein and Volkow (Goldstein & Volkow, 2002) propose an integrated model of substance addiction (I-RISA: Impaired Response Inhibition and Salience Attribution). They suggest that impaired inhibitory control and increased salience to substance cues are the result of activation of frontal cortical areas of the brain during substance cravings and intoxication, and deactivation of these areas during withdrawal. This therefore reinforces drug-seeking right across the addiction lifecycle. Despite their differences, all of these theories, along with Verbruggen et al (Verbruggen, Best, et al., 2014), argue that we must recognise the significance of inhibitory control in motivated behaviours, including the use of alcohol and drugs.

1.6.2 Inhibitory control in the laboratory

The most widely used behavioural measure of inhibitory control is that of response inhibition, which can be measured in the laboratory. These terms are used inter-changeably in the literature and this thesis. Specifically, there are three main task paradigms used throughout the literature to give valid measures of inhibitory control; these are the Stop-

Signal task (Logan et al., 1984), the Go/No-go task (Newman & Kosson, 1986) and the Anti-Saccade task (Hallett, 1978). Each of these tasks measure a somewhat different index of response inhibition (e.g. motor vs. oculomotor), which are further detailed below. Importantly, the focus on response inhibition is key to providing an objective and unbiased behavioural measure of inhibitory control as other self-control measures are questionnaire based, meaning respondents have to identify their behavioural tendencies and report these, which could lead to inaccuracies or biases (Reynolds, Richards, & de Wit, 2006). Indeed, research has demonstrated poor convergent validity between tasks measuring inhibition (e.g. Stroop task) and questionnaire measures of self-control (e.g. (Saunders, Milyavskaya, Etz, Randles, & Inzlicht, 2018)), and that self-report and behavioural measures of impulsivity are distinct and unrelated (Eisenberg et al., 2019; Reynolds, Ortengren, Richards, & de Wit, 2006).

The Stop-Signal task (Logan et al., 1984)

One of the most popular measures of response inhibition involves using the Stop-Signal paradigm (Logan et al., 1984). During these tasks, participants are required to perform a forced-choice reaction time response to certain stimuli (e.g. press the left arrow key if a square appears, press the right arrow key if a circle appears as quickly as possible). These are referred to as no-signal trials or go-trials, and occur uninterrupted on the majority of trials. However, participants are also required to withhold their response on a minority of the trials (stop-signal trials). During these trials, a stop-signal is presented in the form usually of an auditory tone (e.g. a loud beep) or visual signal (e.g. a red cross), which indicates to the participant that they should try to withhold their response on that trial. The most popular paradigm used to describe performance during a Stop-Signal task is the independent horse race model (Logan et al., 1984). The idea behind this is that there is a race between the presentation of the no-signal stimuli (the no-signal process/go process) and the presentation of the stop-signal (the stop process). Therefore, on a stop-signal trial, if the stop process is completed before the no-signal process, then the response is usually withheld suggesting response inhibition is successful. However, if the no-signal process is completed before the stop process, then the response is not withheld i.e. response inhibition is not successful (Verbruggen & Logan, 2009a). During these tasks, the percentage of stop-signal trials is usually around 25% to 33% in order to keep the no-signal response dominant (pre-potent), however this can be altered to increase or decrease the difficulty of the task. Importantly, participants should be informed that they should respond as quickly as possible and not wait

for the stop-signal to appear (Verbruggen et al., 2019), as waiting is thought to reduce the reliability of the response inhibition measure (discussed below) (Verbruggen, Chambers, & Logan, 2013). It is also recommended by Verbruggen et al (Verbruggen et al., 2019) to use a tracking procedure to implement stop-signal delays where possible rather than the traditional fixed delays (Logan et al., 1984). This refers to the delay between presentation of the target stimuli and the stop-signal. When using a tracking procedure, the stop-signal delays are adjusted on a trial-by-trial basis (Verbruggen & Logan, 2009a). Therefore, the initial delay may be 250 ms, but if a participant failed to inhibit the delay would decrease by 50 ms making subsequent inhibition easier. Alternatively, if a participant successfully inhibited, the delay would increase by 50 ms making subsequent inhibition more difficult, as the longer the delay between the presentation of the stimuli and stop-signal, the harder it is to inhibit (Verbruggen, Best, et al., 2014). The index of response inhibition taken from this task is usually the Stop-Signal Reaction Time (SSRT). This refers to the time taken to withhold a response following the presentation of a stop-signal (Brevers et al., 2017), which is calculated from the probability of withholding a response at various stop-signal delays (Smith, Mattick, Jamadar, & Iredale, 2014). These tasks also allow variation in the stimuli used (e.g. neutral or arbitrary stimuli vs. substance-related stimuli), although a two-choice response time task is suggested to be appropriate for the majority of populations (e.g. discriminating between left/right arrows or two pictures) (Verbruggen et al., 2019). However, there is also the opportunity to incorporate relevant cues or distractors (Verbruggen & Logan, 2009b) into the background of the task to investigate if these impair performance.

Go/No-Go task (Newman & Kosson, 1986)

Another popular paradigm used to measure response inhibition is that of Go/No-go tasks (Newman & Kosson, 1986). During these, participants are required to respond to the presentation of 'Go' stimuli (Luijten, Littel, & Franken, 2011). This is usually a motor reaction, for example, pressing a certain button on a keyboard (Meule, 2017). Conversely, participants have to withhold their response to the 'No-Go' stimuli. Typically, 'Go' trials are presented frequently to participants, whereas the 'No-Go' stimuli are presented infrequently (Luijten et al., 2011). The idea of this is for the response to 'Go' trials to become pre-potent. As a result, inhibitory control is inferred from the number or proportion of commission errors; this refers to when participants respond to the 'No-Go' stimuli. Researchers can also calculate response times to 'Go' stimuli as well as the number of correct responses to 'Go'

trials (also known as hits), and the number of incorrect responses where participants fail to press the key (omission errors) when 'Go' stimuli are presented (Meule, 2017).

These tasks can also be modified in similar ways to Stop-Signal tasks. For example, a cue to indicate inhibition is more likely on certain trials can be added. Task difficulty can also be increased by reducing the proportion of No-go trials or requiring participants to respond to Go trials very quickly by providing a target reaction time (Smith et al., 2014). The main difference in comparison to a Stop-Signal task is that the no-go signal usually occurs concurrently with or in place of the go-signal. However, in a Stop-Signal task the stop-signal occurs after the no-signal stimuli has already been presented so that the participant has already began selecting and executing their action (Littman & Takacs, 2017; Smith et al., 2014). This difference has resulted in the suggestion that there are two forms of inhibitory control at minimum. These are *action restraint*, used in Go/No-go tasks whereby the decision to inhibit a response is made from the start. The other type is known as *action cancellation*, which is used during Stop-Signal tasks (and Anti-Saccade tasks), as the decision to inhibit a response takes place after the pre-potent stimuli is presented (Jones, Di Lemma, et al., 2016; Verbruggen & Logan, 2008). Furthermore, SSRT cannot be calculated from performance in Go/No-go tasks as we are unable to calculate the time needed to inhibit a response (as the decision to inhibit is made on initial stimulus presentation). Lastly, in Stop-Signal tasks the speed of go and stop responses are thought to be independent (Logan et al., 1984). Therefore, slower SSRTs are considered to be impairments in inhibitory control whereas slower go responses are considered to be the result of poor attention. Consequently, SSRTs are not influenced by the pattern of go responses (Smith et al., 2014).

Anti-Saccade task (Everling & Fischer, 1998)

Another well-quantified task used to measure inhibitory control is the Anti-Saccade task (Everling & Fischer, 1998). This task is used to measure oculomotor inhibition (eye movements) (Jones & Field, 2015) rather than manual response inhibition, and is well correlated with neurophysiological measures of executive function (Mirsky et al., 2011). In this task, participants are typically required to provide an automatic saccade to a target stimulus or location (pro-saccade), or a saccade to the opposite stimulus or location (anti-saccade), which is reflective of inhibition (Campbell, Chambers, Allen, Hedge, & Sumner, 2017). For example, participants may first be shown an image on either side of the screen. Following this, a target stimuli (e.g. an arrow pointing in 1 of 4 directions) is briefly

presented for a short time on the opposite side of the screen to which the image was presented. Participants are then required to provide a key press to suggest which direction the arrow was facing. Therefore, to increase the likelihood of providing a correct response, participants are required to try and inhibit their natural response to look at the image first presented, as the target stimuli is only presented briefly (Jones & Field, 2015).

1.7 Executive functioning and Impulsivity in substance use

The ability to carry out and adapt goal-directed behaviour is suggested to be the product of executive control (Verbruggen, McLaren, & Chambers, 2014). This term refers to a variety of higher order cognitive capabilities, for example, planning behaviour, inhibition and decision making which enable individuals to self-regulate and control more complex behaviours (Miyake et al., 2000). Inhibitory control is therefore regarded as a key executive function as the inhibition of an inappropriate response allows the individual time to move towards a more appropriate action or behaviour (e.g. individuals may suppress an initial response to think about the consequences of their next action or behaviour (Smith et al., 2014)).

Working memory processes are also thought to support behavioural control and self-regulation (Fillmore, 2003; Finn, 2002). Working Memory Capacity (WMC) is defined as a brain system which allows provisional storage of information that is essential for complex cognitive abilities including learning, reasoning and language comprehension (Baddeley, 1992). Although, some models (e.g. 'The Unity/Diversity framework' (Miyake & Friedman, 2012)) suggest that inhibitory control is subsumed under a common executive function variable which represents the ability to maintain task-related information and goals. Nevertheless, it has been suggested that the same brain mechanisms may underlie the etiologies of certain psychiatric disorders and Substance Use Disorders due to observed deficits in both inhibition and WMC (Grégoire, Rivalan, Le Moine, & Dellu-Hagedorn, 2012). Certainly, Finn (Finn, 2002) suggests that individual differences in WMC may contribute to impulsivity and the accompanying behavioural issues such as alcohol misuse and abuse.

Contemporary models of addiction suggest that increased impulsivity has a key role in alcohol addiction, with impulsivity being regarded as both a determinant and a consequence of substance misuse (de Wit, 2009; Weafer, Mitchell, & de Wit, 2014). Impulsivity was originally referred to as a quick reaction to stimuli both internally and externally without thinking or having any regard for the consequences of actions (Dawe &

Loxton, 2004). However, impulsivity now tends to be referred to as multi-dimensional, or an umbrella term for traits which capture various aspects of behaviour, for example delay discounting, risk-taking and indeed response inhibition (Weafer & Fillmore, 2016). However, there is still some disagreement on the best way to conceptualise and measure impulsivity (Christiansen, Cole, Goudie, & Field, 2012), with multiple definitions having been recommended (Bakhshani, 2014).

Nevertheless, research has demonstrated that trait impulsivity is associated with Alcohol Use Disorders (e.g. (von Diemen, Bassani, Fuchs, Maciel Szobot, & Pechansky, 2008)) and is a risk factor for hazardous drinking (Christiansen, Cole, Goudie, et al., 2012; Fernie et al., 2013). These measures of trait impulsivity tend to be questionnaire based (e.g. The Barratt Impulsivity Scale (BIS; (Patton, Stanford, & Barratt, 1995) see Appendices 1.E), and conceptualise impulsivity as a stable trait. However, alcohol intoxication is also suggested to cause both acute and chronic fluctuations in components of impulsivity (de Wit, 2009), and can also influence other executive functions such as decision-making and inhibitory control whilst under the influence (Fillmore, 2003; Weafer & Fillmore, 2016). Supporting this, it has been suggested there are two independent measures of impulsivity; the first is inhibitory control, which as discussed, is most frequently measured by the Stop-Signal (Logan et al., 1984) and Go/No Go tasks (Newman & Kosson, 1986), and the second is impulsive decision making (also referred to as delay discounting) which is most often measured by Delay-Discounting tasks (Madden, Petry, Badger, & Bickel, 1997). This concept refers to over-sensitivity to rewards received immediately, and de-valuation of delayed rewards (Matta, Gonçalves, & Bizarro, 2012). Both of these components can be measured using objective, behavioural tasks rather than questionnaire based measures. Importantly, research has supported this distinction (e.g. (Christiansen, Cole, Goudie, et al., 2012; Reynolds, Ortengren, et al., 2006)) using Principal Component Analyses to demonstrate independent measures of inhibitory control and impulsive decision making, across Delay-Discounting tasks and response inhibition tasks. Christiansen et al (Christiansen, Cole, Goudie, et al., 2012) also found a third independent component, which represented trait impulsivity (as measured by the BIS), in support of other research demonstrating behavioural measures of impulsivity and self-report measures are distinct (Eisenberg et al., 2019; Reynolds, Ortengren, et al., 2006). More importantly, each of the three independent measures in this study predicted unique variance in hazardous alcohol consumption.

Similarly, in a review conducted by Bickel et al (Bickel, Jarmolowicz, Mueller, Gatchalian, & McClure, 2012), they separated the construct of impulsivity into a trait and four states, that is attention deficit impulsivity, impulsive choice, disinhibition and reflection impulsivity. Each aspect is thought to have its individual psychobiology and etiology (Papachristou, Nederkoorn, Corstjens, & Jansen, 2012), and is implicated in substance dependence (Weafer & Fillmore, 2016) and other disorders such as Schizophrenia and ADHD (Bari & Robbins, 2013). Although, it should be noted that not every behaviour considered impulsive is detrimental or harmful, and actually a slight "loss of control" can be advantageous in some situations (Bari & Robbins, 2013) (e.g. when a quick decision is required in a pressured situation (Herman, Critchley, & Duka, 2018)).

Importantly, Bickel et al suggested that specific components of executive functions are an antipode to components of impulsivity. They argued that behavioural disinhibition (i.e. the (in)ability to restrain a behaviour that has already been initiated, often associated with impulsive and norm-violating behaviour (Bogg & Finn, 2010)) is the antipode of behavioural inhibition (i.e. an executive function that describes three related processes; (i) inhibition of a prepotent response, (ii) withholding an ongoing response to delay the decision to respond and (iii) inference control (Barkley, 1997)). Specifically, Bickel et al (Bickel et al., 2012) argue that behavioural disinhibition is implicit in the second process described above. Therefore, effective performance on a Stop-Signal task could be taken to represent low impulsivity and efficient executive functioning. Conversely, poor performance could represent higher or dysfunctional impulsivity and inefficient executive functioning. As such, components of executive functioning and impulsivity may operate at opposite ends of an identical scale (Bickel et al., 2012). Indeed, if an individual did not experience a strong urge, they would not need to inhibit their response, or if the individual had good inhibition, the impulsive behaviour would be inhibited (Bari & Robbins, 2013). Supporting evidence for this (e.g. (Castro-Meneses, Johnson, & Sowman, 2015)) has demonstrated that individuals with high or dysfunctional impulsivity have slower SSRTs compared to individuals with lower impulsivity scores. However, there is a lack of overlapping research between these two constructs (Bickel et al., 2012) and some of the existing literature has reported "null" findings (e.g. (Lijffijt et al., 2004)).

1.8 Development of inhibitory control

Whilst trait impulsivity is thought to have an innate factor (Kreek, Nielsen, Butelman, & LaForge, 2005), or often decrease throughout adulthood (Forrest, Hay, Widdowson, & Rocque, 2019), the ability to inhibit incongruous behaviour is thought to develop more gradually throughout childhood and into adulthood. Indeed, an understanding of the development of inhibitory control is important in the context of substance addiction. This is because some evidence suggests that early interventions in those with poor inhibitory control could be particularly useful in helping to recognise young individuals who are at risk of developing Substance Use Disorders (Moeller et al., 2016). Certainly, most research investigating the development of effective inhibition has focused on the transition from young children to adolescents (e.g. (Conners, Epstein, Angold, & Klaric, 2003; Tillman, Thorell, Brocki, & Bohlin, 2008; Williams, Ponesse, Schachar, Logan, & Tannock, 1999)). These studies tend to demonstrate that behavioural indexes of inhibition improve significantly over this period (Petersen, Hoyniak, McQuillan, Bates, & Staples, 2016). For example, using a Go/No-Go task, one study (Williams et al., 1999) demonstrated that stopping speed became quicker with increasing age during childhood, with little evidence of this slowing during adulthood. Another study (Tillman et al., 2008) also demonstrated that inhibition developed with age in 4-12 year olds using a Stop-Signal task. This suggested that inhibition was improving until a minimum age of 12 years. Other research (e.g. (Luna et al., 2001)) has suggested that adult-like inhibitory control matures progressively through childhood and adolescence, although the age at which inhibitory control is fully developed often depends on task difficulty. For example, on simple inhibitory tasks young children may display adult-like inhibition. Whereas, inhibition may gradually develop until adolescence on tasks which are more complex and involve the use of other cognitive functions (Petersen et al., 2016).

Nevertheless, the most likely explanation for the slow development of inhibitory control is due to the maturation of the brain. Research suggests that the development of the Prefrontal Cortex (PFC) underlies the maturation of inhibitory control (Munakata et al., 2011). For example, research using imaging techniques (e.g. (Casey et al., 1997; Tamm, Menon, & Reiss, 2002)) demonstrated that inhibition during a Go/No-Go task correlated with increased activation in the PFC. Furthermore, the level of activation was increased in children compared to adults which may be as a greater effort is required for children to inhibit their responses. Another study (Durston et al., 2002) reported that brain activity contrasted

between children and adults during a Go/No-Go task. Specifically, there was increased activation in the parietal and prefrontal regions in children compared to adults. However, their results also suggested that the ventral fronto-striatal circuitry may play a role in the development of inhibition in children between 6-10 years old. Luna et al (Luna et al., 2001) also investigated this in 8-30 year olds. They demonstrated that activation of the PFC was increased in adolescents compared to adults or younger children. There was also progressively increasing activation in frontal, thalamic, striatal and parietal regions of the brain from children to adults. They suggested that the maturation of these brain areas underlies the improvement of inhibitory control, which may not be entirely developed until adulthood.

However, Aron et al (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003) comment that it is difficult to specifically locate the areas responsible for executive functions in the PFC. They compared healthy controls to individuals with a right Inferior frontal cortex (rIFG) lesion and found this area to be key in relation to inhibitory control. Other research using Go/No-Go and Stop-Signal tasks has supported the function of the rIFG in inhibition (e.g. (Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010; Rubia, Smith, Brammer, & Taylor, 2003), as has a review of the literature (Aron, Robbins, & Poldrack, 2014).

1.9 Inhibitory control in substance use

1.9.1 Alcohol-dependent patients

Importantly, much research using Stop-Signal and/or Go/No-go tasks has demonstrated poorer inhibitory control in those with an alcohol dependency, compared to healthy controls (Goudriaan et al., 2006; Lawrence, Luty, Bogdan, Sahakian, & Clark, 2009; Zago-Gomes Mda & Nakamura-Palacios, 2009). This evidence is supported by meta-analyses which show inhibitory control is impaired in alcohol dependent patients and heavy drinkers compared to healthy controls (Smith et al., 2014), and that the broader construct of impulsivity is a robust characteristic in individuals who are dependent on alcohol or other stimulants and opiates (Verdejo-García, Lawrence, & Clark, 2008). Poor inhibitory control has also been related to cigarette dependency (Billieux et al., 2010), and has been demonstrated in cocaine (Fillmore & Rush, 2002) and methamphetamine (Monterosso, Aron, Cordova, Xu, & London, 2005) users compared to control groups. However, there are some studies which have reported no differences between healthy controls and those with a current diagnosis of alcohol

dependence (van der Plas, Crone, van den Wildenberg, Tranel, & Bechara, 2009) or a history of alcohol dependence (Taylor et al., 2016).

Despite this, longitudinal evidence suggests that inhibitory control deficits contribute to the development of alcohol dependence (e.g. (Fillmore, 2003; Rubio et al., 2008)), comorbid drug and alcohol use (Nigg et al., 2006), as well as treatment success (Rupp et al., 2016). One study (Czapla et al., 2016) also reported that alcohol dependent patients had worse inhibitory control than healthy controls and that the likelihood of relapse at a 6-month follow up was predicted by individual differences in inhibitory control. Specifically, those with the largest impairments in inhibition and a high number of past detoxifications posed the biggest risk for relapse. However, it has also been demonstrated that impairments in inhibitory control may exist before alcohol use develops (Ersche et al., 2012; Moeller, Bederson, Alia-Klein, & Goldstein, 2016), suggesting that they may play a causal role in alcohol dependence. Certainly, high levels of impulsivity are said to exist prior to drug use in substance dependent populations which increases vulnerability to drug use and dependence. However, there is also strong evidence to suggest that the use of alcohol and drugs has an effect on both brain structures and functioning in the long-term, which may hide these pre-existing characteristics (Verdejo-García et al., 2008).

1.9.2 Non-dependent drinkers

There is also a substantial body of evidence, which indicates that impairments in inhibitory control are related to alcohol use in non-dependent drinkers (e.g. (Christiansen, Cole, Goudie, et al., 2012; Colder & O'Connor, 2002; Houston et al., 2014; Murphy & Garavan, 2011)). Certainly, these impairments have been associated with binge drinking (Carbia, Lopez-Caneda, Corral, & Cadaveira, 2018), *ad libitum* alcohol consumption in laboratory studies (Field & Jones, 2017; Jones, Field, Christiansen, & Stancak, 2013; Weafer & Fillmore, 2008), as well as the number of intoxication and hangover days in young adults (Paz, Keim, & Rosselli, 2016). Longitudinal studies (e.g. (Fernie et al., 2013)) have also reported that individual differences in inhibitory control in adolescents predict involvement with alcohol after six months. However, there was no evidence that heavy alcohol use worsened inhibitory control in these adolescents. Furthermore, Hu et al (Hu, Zhang, Chao, Krystal, & Li, 2016) reported that higher scores on the Alcohol Use Disorders Identification Test (AUDIT) were associated with worse response inhibition during a Stop-Signal task in social drinkers.

However, this correlation was only moderate (r=.38) and there was no difference in response inhibition between these individuals and those who reported abstinence from alcohol.

As such, a meta-analyses by Smith et al (Smith et al., 2014) suggested that although deficits in inhibitory control are evident in heavy drinkers, these deficits were less evident compared to those in dependent drinkers. Certainly, it should be noted that there are numerous studies which have failed to find a relationship between individual differences in inhibitory control and alcohol consumption (e.g. (Fernie, Cole, Goudie, & Field, 2010)). For example, one study (Bø & Landro, 2017) reported the opposite relationship to what was expected i.e. weekly alcohol use was related to better inhibitory control (compared to alcohol abstinence) in a sample of the general public. This could suggest that the relationship between impairments in inhibitory control and alcohol use is restricted to certain populations or a specific developmental phase, as the majority of research focuses on heavy drinking university students or young adults. However, the sample in this study generally displayed between low and moderate levels of drinking which could also explain the results. Nevertheless, other studies have also demonstrated very little evidence of inhibitory control deficits in heavy drinkers (e.g. (Bednarski et al., 2012; Franken, Luijten, van der Veen, & van Strien, 2017; Nederkoorn, Baltus, Guerrieri, & Wiers, 2009)), or binge drinkers (e.g. (Czapla et al., 2015; Moreno et al., 2012)) compared to controls. Although Czapla et al (Czapla et al., 2015) did report that binge drinking was associated with increased commission errors during a Go/No-Go task.

1.9.3 Neurophysiological evidence

Regardless, as well as the behavioural evidence there is also neurophysiological research which has investigated the relationship between alcohol use and inhibitory control in both non-dependent and dependent drinkers. This offers a more sensitive measure than behavioural data (e.g. reaction times, accuracy), which can be volatile in nature and influenced by a variety of factors (e,g. hardware delays (Woods, Wyma, Yund, Herron, & Reed, 2015) or past experience of similar tasks (Wong, Goldsmith, Forrence, Haith, & Krakauer, 2017)). The majority of this research focuses on two event-related potential (ERP) components; N200 and P300, which have been associated with two aspects of inhibitory control (Enriquez-Geppert, Konrad, Pantev, & Huster, 2010; Huster, Enriquez-Geppert, Lavallee, Falkenstein, & Herrmann, 2013; Liu et al., 2015). Specifically, the P300 is a positive component which peaks at around 300-350ms following a stop-signal (Dimoska,

Johnstone, Barry, & Clarke, 2003; Jones, Field, et al., 2013), and is therefore thought to represent the final stages of response inhibition (Wessel & Aron, 2015). Whereas, the N200 is a negative component which peaks around 200-250ms following presentation of a stop-signal. However the functional specificity of the N200 component still has a degree of uncertainty (Dimoska, Johnstone, & Barry, 2006), with the possibility it is related to response conflict or error monitoring (Donkers & van Boxtel, 2004; Enriquez-Geppert et al., 2010; Kok, Ramautar, De Ruiter, Band, & Ridderinkhof, 2004; Yeung, Botvinick, & Cohen, 2004). Certainly, when response inhibition is successful, the P300 component has been shown to consistently increase in amplitude more than when inhibition is unsuccessful, whereas the N200 ERP has been shown to have larger amplitudes during failed inhibition (Dimoska et al., 2003; Jones, Field, et al., 2013; Kok et al., 2004).

Crucial evidence has also demonstrated reduced P300 amplitudes during response inhibition could be a marker for vulnerability to alcohol dependency (Hesselbrock, Begleiter, Porjesz, O'Connor, & Bauer, 2001; Kamarajan et al., 2005; Stein, Fey, Koenig, Oehy, & Moggi, 2018). For example, one study (Kamarajan et al., 2005) demonstrated that alcohol dependent individuals displayed reduced P300 amplitudes and different topography when completing a Go/No-go task compared to healthy controls, suggesting that different brain areas may have been activated during response inhibition in those dependent on alcohol. From this, the authors suggested that reduced P300 amplitudes may serve as an endophenotype for Alcohol Use Disorder. Certainly, research has demonstrated that the amplitudes of P300 waves are decreased by moderate measures of alcohol during inhibition tasks (Bartholow et al., 2003; Easdon, Izenberg, Armilio, Yu, & Alain, 2005), and that these amplitudes are related to *ad libitum* alcohol consumption (Jones, Field, et al., 2013).

Contrastingly, increased P300 amplitudes during Go/No-go tasks have also been reported in binge drinkers (Lopez-Caneda et al., 2012). However, the authors suggested this may have been the result of a requirement for increased activation to complete the task in binge drinkers (i.e. these participants had to try harder to successfully inhibit), although there was no behavioural differences between the groups. Other research has also demonstrated decreased N200 amplitudes in alcohol dependent males compared to controls (Pandey et al., 2012), and similar results have been found for other addictive substances. For example, decreased N200 amplitudes during no-go trials have been reported in smokers compared to healthy controls, although there were no distinctions between these groups in amplitudes of P300 in this study (Luijten et al., 2011). Indeed, there is other contradictory evidence. For example, Smith et al (Smith, Iredale, & Mattick, 2016) reported that heavy drinkers showed

marginal differences in P300 amplitudes compared to light drinkers, however on closer inspection this is non-significant (p=.09). Another study (Oddy & Barry, 2009) demonstrated an association between P300 amplitudes on No-Go trials and alcohol consumption. However, the heavy and light drinking groups did not significantly differ on task performance. Thus, the authors suggested that this did not represent impairments in inhibitory control. Consequently, although there is some robust (and longitudinal) behavioural and neurophysiological evidence for the relationship between poor inhibitory control and hazardous drinking, there are also contradictory findings. Certainly, we cannot infer a causal relationship as the majority of research is cross-sectional. As a result, there is controversy in whether poor inhibitory control is a determinant or a consequence of substance use or misuse.

1.10 Inhibitory control as a risk factor or consequence of substance misuse

In a review of the literature, Jones et al (Jones, Christiansen, Nederkoorn, Houben, & Field, 2013) suggest that there are two plausible explanations for the relationship between inhibitory control and alcohol use. The first is that the PFC is subjected to neurotoxic effects due to chronic substance use, and this may impair inhibitory control. Conversely, the second explanation is that poor inhibitory control during adolescence may be a risk factor for developing substance use and eventually a Substance Use Disorder (Jones, Christiansen, et al., 2013). Indeed, another literature review (Perry & Carroll, 2008) argues that there is supporting evidence for both explanations, which are discussed below.

1.10.2 Neurobiological theories: poor inhibitory control as a consequence of chronic substance use

The Incentive Sensitization theory (Robinson & Berridge, 1993) argues that recurring use of substances can lead to abnormalities in the brain reward-related systems that contribute to motivated behaviour. These abnormalities can lead to increased salience of drug-related stimuli which can increase future substance-seeking, even following periods of abstinence (Robinson & Berridge, 2008). Following on from this, Goldstein and Volkow (Goldstein & Volkow, 2002) created their 'Impaired Response Inhibition and Salience Attribution Syndrome of Drug Addiction Model' (I-RISA). They suggested that the frontal cortex is involved in the reinforcement of substance-seeking right across the addiction life-cycle including periods of increased craving, intoxication and withdrawal. This is because recurring

exposure to the substance and its associated cues increases salience and alters brain systems that control behaviour. This therefore results in increased drug use, including both bingeing and relapse.

Evidence supporting these theories has demonstrated that repeated substance use damages brain structures. Indeed, animal studies have shown that following a four day ethanol binge paradigm, adolescent and adult rats experience significant brain damage with increased damage in the frontal cortical regions in the adolescents (Crews, Braun, Hoplight, Switzer III, & Knapp, 2000). Nixon and Crews (Nixon & Crews, 2002) found comparable results suggesting both acute and chronic binges of ethanol leads to decreased cell proliferation in adult male rats. Similar results have been demonstrated in humans. For example, research has demonstrated that heavy non-dependent drinkers posed a higher risk for frontal lobe reduction in comparison to abstainers. However, moderate alcohol use was not associated with frontal lobe reduction (Kubota et al., 2001). Other research has demonstrated that alcohol dependent patients have a damaged PFC (Crews et al., 2004) (which as described above is suggested to underlie inhibitory control functioning), decreased frontal lobe volumes (Pfefferbaum, Sullivan, Mathalon, & Lim, 1997) or decreased grey matter volumes (van Holst, de Ruiter, van den Brink, Veltman, & Goudriaan, 2012) compared to healthy controls.

Importantly, some evidence suggests the brain atrophy is partially reversible after periods of abstinence (Bartsch et al., 2007; Cardenas, Studholme, Gazdzinski, Durazzo, & Meyerhoff, 2007; Gazdzinski, Durazzo, & Meyerhoff, 2005). Certainly, Mann et al (Mann et al., 2005) reported that brain volumes increased in alcohol dependent individuals following only six weeks of abstinence, however these were still reduced compared to the healthy control group. As such, it is still unclear whether the brain can fully recover following long-term abstinence (Zahr & Pfefferbaum, 2017). Regardless of this, there is evidence that substance use may directly lead to impairments in inhibitory control by damaging fontal areas of the brain. These impairments may lead to further substance use behaviour.

1.10.3 Longitudinal theories: poor inhibitory control as a risk factor for substance use

Contrastingly, other research has suggested that impairments in inhibition may exist before Substance Use Disorders develop and may actually predict their onset. In support of this, one study (Ersche et al., 2012) reported irregularities in fronto-stratial brain areas, which are associated with self-control, in both substance addicted individuals and their healthy siblings.

Therefore, they suggested that these brain irregularities related to self-control may predispose individuals to substance addictions. Other longitudinal studies have demonstrated that impairments in inhibitory control during adolescence or childhood are a risk factor for developing later alcohol problems (Mahmood et al., 2013; Nigg et al., 2006; Tarter, Kirisci, Habeych, Reynolds, & Vanyukov, 2004; Wong et al., 2006). For example, one study (Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014) reported that deficits in inhibitory control before substance use began (in aged 12-14 year olds) was associated with increased alcohol use (measured as number of drinking days and number of drinks per occasion) and marijuana use in a follow-up during late adolescence (aged 17-18).

Comparable results have been reported in adults. For example, Rubio et al (Rubio et al., 2008) reported that impaired inhibition predicted the transition from heavy drinking to Alcohol Use Disorder at a four year follow-up. Another study of alcohol-dependent patients demonstrated that poorer response inhibition during a Go/No-Go task was a risk-factor for dropping out of treatments and relapse (Rupp et al., 2016). Therefore, it is possible that poor inhibitory control is a vulnerability marker for alcohol misuse later in life. Certainly, there is robust, longitudinal support for the relationship between impaired inhibitory control during childhood and adolescence and the progression of Substance Use Disorders.

Nevertheless, some research argues that inhibitory control deficits (and the associated fronto-striatal circuit differences) may both precede and occur following excessive substance use (Morein-Zamir & Robbins, 2015). Certainly, the notion that inhibitory functions are still developing during adolescence may place these individuals at risk for alcohol misuse. However, alcohol misuse may also interfere with the development of inhibitory functions resulting in reduced control of intake. Furthermore, Perry and Carrol (Perry & Carroll, 2008) also suggest an alternative hypothesis that impulsive behaviour is related to substance addiction through a third common factor (e.g. sex, environment, reward reactivity). Thus, it is only with additional longitudinal studies that we can fully understand the causal relationship between inhibitory control and alcohol addiction (López-Caneda, Rodríguez Holguín, Cadaveira, Corral, & Doallo, 2013).

1.11 Over-simplification of inhibitory control

To summarise so far, inhibitory control is implicated as an important construct in alcohol misuse and addiction, and there is substantial evidence to support this. However, as described above there are also inconsistent results across the literature, with many studies also lacking

statistical power (Smith et al., 2014). This is not just the case in the addiction literature, Verbruggen and colleagues (Verbruggen, McLaren, et al., 2014) argue that although inhibitory control (and other executive functions) have been the focus of much literature in various other disciplines, understanding remains to be inadequate. Consequently, Verbruggen et al (Verbruggen, McLaren, et al., 2014) have developed a theoretical framework which aims to look more specifically at the processes involved in response inhibition. Indeed, they suggest that researchers often fail to question the mechanistic processes which underlie the function they are investigating, and instead state that group differences are the product of deficits in "inhibition" or increasingly general terms such as impairments in "executive functions." Therefore, research in this form does not explain which specific underlying processes are contributing to group differences and cannot further our understanding.

When using Stop-Signal tasks, researchers typically measure differences in SSRT or the frequency of errors to operationalise differences between conditions or groups in inhibitory control (Verbruggen, McLaren, et al., 2014). Therefore, performance is generally ascribed to a single function of inhibitory control. However, reactive stopping involves multiple processes that allow an individual to stop successfully, rather than simply the duration of the single stopping process (Verbruggen, McLaren, et al., 2014). To be specific, as well as a final motor-related process (the 'reactive' act of inhibiting or not), reactive stopping involves both perceptual and decisional processes (Elchlepp, Lavric, Chambers, & Verbruggen, 2016).To give a real-life example, reactive stopping in a car involves detection of a stop-signal (e.g. a pedastrian or object in the road), followed by the selection of an action (e.g. press the break pedal) and the execution of an action (e.g. move foot onto the break pedal) (Verbruggen, McLaren, et al., 2014). Therefore, by attributing performance on Stop-Signal tasks (and other task paradigms) to a general inhibitory deficit, rather than acknowledging these underlying processes, we are not providing an in depth explanation of performance. These processes are described in more detail below.

1.11.1 Signal detection

In Verbruggen et al's (Verbruggen, McLaren, et al., 2014) framework, they suggest that signal detection is the first stage of the inhibitory process (e.g. detecting an auditory tone in a Stop-Signal task or a red traffic light in the real world). This is an important process as if the signal is not detected rapidly enough or detected at all, there can be adverse effects (e.g. failing to inhibit in a Stop-Signal task or going through a red light), the severity of which

depends on the environmental context. Verbruggen et al (Verbruggen, Stevens, & Chambers, 2014) demonstrated this in a recent study in which participants completed a Stop-Signal task which required them to detect a stop-signal presented either centrally in the screen or in the periphery of the screen. There were also perceptual distractors presented on some of the trials. Importantly, Verbruggen and colleagues demonstrated that the distractors lead to impairments in response inhibition, particularly when the stop-signals were presented in the periphery of the screen. This suggests that stop-signals are harder to detect when presented away from the focus of participants (i.e. in the periphery of the screen) and in the presence of distractors, which can have a negative effect on inhibition performance. Therefore, signal detection may be essential for effective stopping.

This concept also generalises to response inhibition outside of the laboratory. Indeed, individuals outside of the laboratory are regularly required to detect inhibitory signals in noisy surroundings (e.g. on a busy junction). Thus, the capacity to detect a stop-signal amongst other distractors rapidly may be essential in successful and efficient inhibition (Verbruggen, McLaren et al., 2014). This also may have particular relevance for substance use behaviour. For example if a heavy drinker is intoxicated or in an substance-cue rich environment, their selective attention may be directed towards the substance-related cues (Field et al., 2016) or impaired due to intoxication (Plawecki, Koskie, Kosobud, Justiss, & O'Connor, 2018; Roberts, Miller, Weafer, & Fillmore, 2014). This may make it harder for them to detect inhibitory signals (e.g. Others reacting negatively towards them due to signs of intoxication such as talking loudly, stumbling) and lead to higher alcohol intake. Consequently, Verbruggen et al (Verbruggen, McLaren, et al., 2014) argue that at the minimum, some variance in inhibitory control is related to the ability to detect inhibitory signals in the environment. Yet despite this, group differences in stopping performance are generally attributed to the inhibition of motor responses with the influence of signal detection regularly overlooked.

1.11.2 Action selection

Following the detection of a cue or stop-signal is the requirement to select an appropriate action (or response) to meet the appropriate goal-directed behaviour (Bender, Filmer, Garner, Naughtin, & Dux, 2016; Verbruggen, McLaren, et al., 2014). The numerous stages of action selection have been described by Sequential-Sampling models and according to these, action selection depends on the collection of information from the environment until sufficient

information is gathered to support the selection of a certain action (Ratcliff & Smith, 2004). This collection of evidence may be slower amongst noise in the environment (e.g. the presence of distractors) or the internal cognitive system (e.g. multiple ongoing processes). This may lead to a longer action selection process and therefore slower response times and poorer accuracy (Verbruggen, McLaren, et al., 2014). Furthermore as discussed above, individuals require the ability to withhold inappropriate actions if they are to prevent impulsive actions and follow goal-directed behaviour (Rae, Hughes, Weaver, Anderson, & Rowe, 2014). Interestingly, Verbruggen et al (Verbruggen, McLaren, et al., 2014) argue that comparable stages occur during the withholding of responses to that which are described above. Indeed, the preceding context may suggest that an action is unsuitable before the response is activated (Rae et al., 2014).

1.11.3 Action execution

Finally, the chosen action must be performed. This involves the formation of a motor sequence to perform the action which may lead to an interval between action selection and action execution (Verbruggen, McLaren, et al., 2014). As described above, individuals are sometimes required to withhold inappropriate actions. Information that a response needs to be withheld can occur after an action has already been selected. However, this action can still be withheld or adapted (Verbruggen & Logan, 2009b) (e.g. when a stop-signal is presented in a Stop-Signal task instructing the participants to cancel the go-response (Rae et al., 2014)). Taking all of this into account, it is clear that multiple processes are involved in successful reactive stopping.

1.11.4 Proactive control

In addition, it has also been suggested that successful inhibition of a response not only requires reactive control, but is also the result of preparation through proactive control processes (Criaud, Wardak, Ben Hamed, Ballanger, & Boulinguez, 2012). Importantly, the three stages described above are suggested to be influenced by these processes as well as learning. Verbruggen and colleagues suggest that we must recognise the influence of these processes otherwise we risk providing an incomplete model of inhibitory control (Verbruggen, McLaren, et al., 2014; Verbruggen, Stevens, et al., 2014). Specifically, Verbruggen et al (Verbruggen, McLaren, et al., 2014) note that much of the past inhibitory control literature focuses on ‘reactive’ inhibitory control (the act of stopping), however we

are also able to plan and modify our behaviour proactively. This is also reflected in the Dual Mechanisms of Control (DMC) framework (Braver, 2012) which argues that inhibitory control can be operationalised into reactive control (retrieving contextual information only when required in the 'here and now') and proactive control (actively maintaining contextual information to prepare a response).

To give a real-world example, if you think about driving a car when you notice another vehicle about to pull out into your pathway. You could either prepare yourself to perform an emergency stop or avoid preparation and just take note that the vehicle is going to pull out. Then when it does pull out, try to stop at the very last moment of opportunity. Taking this example, preparation would be safer as otherwise you would have to respond very quickly to stop and avoid an accident with the other vehicle (Richmond, Redick, & Braver, 2015). Importantly, Aron (Aron, 2011) suggests that 'proactive' control may offer a more appropriate model of inhibition in substance use behaviours, and other research has gone as far to suggest that proactive control is the default mode of inhibitory control (Criaud et al., 2012). Theoretically, it seems more plausible that individuals trying to regulate substance use would proactively adjust their behaviour over time to control their cravings (e.g. preparing to decline an offer for a drink), rather than relying on reactive control as a late correction mechanism (e.g. reaching for a bottle then inhibiting) (Braver, 2012; Braver, Paxton, Locke, & Barch, 2009). However, there is a lack of research, which investigates the relationship between proactive control and substance misuse.

Importantly, research using Stop-Signal tasks have recently been adapted to disentangle reactive control from proactive control and allow separate measurement. During these tasks, participants are asked to respond as quickly as possible rather than waiting for the stop-signal to appear (Logan et al., 1984). However, research has demonstrated that participants slow down their responses as stop-signal probability increases (Verbruggen, Liefooghe, Notebaert, & Vandierendonck, 2005; Verbruggen, Liefooghe, & Vandierendonck, 2006). For example, Verbruggen et al (Verbruggen, Stevens, et al., 2014) incorporated a block of trials without stop-signals in their Stop-Signal task and investigated whether participants responded faster during this block (i.e. where no inhibition was required) compared to the blocks which included stop-signals (i.e. where response inhibition was required). Results revealed that participants slowed down their responses when inhibition was required suggesting they proactively adjusted their behaviour (Verbruggen & Logan, 2009b). This is supported by further research demonstrating that participants prepare themselves to detect stop-signals through proactive adjustments of their behaviour (Elchlepp et al., 2016;

Verbruggen & Logan, 2009b; Zandbelt, Van Buuren, Kahn, & Vink, 2011). Importantly, one study, (Hu, Ide, Zhang, Sinha, & Li, 2015) demonstrated that a lower number of alcohol dependent patients (compared to controls) slowed down their responses as stop-signal probability increased suggesting poorer proactive control, whereas, there was no differences in SSRTs.

Other research has incorporated a stop-signal cue to indicate stop-signal probability (e.g. (Brevers et al., 2017; Verbruggen & Logan, 2009b)). Here, the index of proactive inhibition is measured by the proportion of inhibition errors. Hence, when using either adaptation, reactive control is still operationalised as SSRT (outright stopping) but proactive control is operationalised as the preparation to stop in the anticipation of stop-signals (Castro-Meneses et al., 2015). This research, along with other studies (e.g. (Castro-Meneses et al., 2015; Jahfari, Stinear, Claffey, Verbruggen, & Aron, 2010), have also demonstrated how increased preparation is association with faster SSRTs, suggesting that preparation has a downstream effect on reactive inhibition. This may be because the same inhibition network that is activated when reactive stopping is required is pre-activated by proactive adjustments, allowing participants to withhold their responses quickly (Castro-Meneses et al., 2015).

To summarise so far, Verbruggen et al's (Verbruggen, McLaren, et al., 2014) framework suggests that inhibition can be broken down into three basic processes, that is, signal detection, action selection and action execution. These processes are also modulated by other processes such as proactive control (i.e. preparation). Therefore, in order to develop our understanding and give a more specific explanation of inhibitory control, we should focus our research on these underlying processes rather than a general impairment in inhibitory control or executive functions. To my knowledge there is a very limited number of studies which have investigated the relationship between proactive control and/or signal detection and heavy drinking, two processes which may have particular relevance to substance misuse. Therefore, a key aim of my thesis was to investigate these relationships. Furthermore, the mechanisms underlying the relationships between inhibitory control and hazardous drinking are also poorly understood. Below I discuss two potential mechanisms that may underlie the preparation of responses (i.e. proactive control) and that could explain individual differences in the ability to implement proactive control.

1.11.5 Alcohol sensitivity

Firstly, a low sensitivity (LS) to alcohol is thought to be a risk factor for alcohol misuse and dependence (Fleming & Bartholow, 2014; Schuckit & Smith, 2000). This is because individuals with a low response to the acute effects of alcohol may consume more alcohol per drinking session in order to experience the desired effects (Schuckit et al., 2011). In support of this, a meta-analysis (Quinn & Fromme, 2011) reported that heavy drinkers (compared to light drinkers) were less sensitive to the sedating effects of alcohol but more sensitive to the stimulating effects of alcohol. Alcohol sensitivity can be measured by the quantity of alcohol required to feel its acute effects through a self-report measure (as described in Chapter two General Methods) or through measurement of blood alcohol concentration after consuming a dose of alcohol (Schuckit et al., 2011). Importantly, research has demonstrated that relatives of those with alcohol dependency exhibit significantly lower responses to alcohol compared to healthy controls (Kareken et al., 2013; Schuckit et al., 2000). Other evidence has suggested that a LS to alcohol partially mediates the association between a family history of alcohol dependence and the development of alcohol dependence (Schuckit & Smith, 1996). Indeed, in a more recent study (Schuckit & Smith, 2000), these authors reported there was a robust association between a low response to alcohol and Alcohol Use Disorders.

Alongside this, research measuring event-related potentials has shown that alcohol-related stimuli especially attract the attention of those who self-report LS to alcohol (e.g. (Bartholow, Lust, & Tragesser, 2010; Fleming & Bartholow, 2014)). In one study (Bailey & Bartholow, 2016), university students were required to complete an Alcohol-Stroop task in which they completed two blocks; one of which involved mostly neutral words and one of which consisted of mostly alcohol words. Importantly, those with a LS to alcohol were slower to respond and more accurate when responding to alcohol words in the mostly neutral block, suggesting they were able to utilise reactive control when conflict was occasional (as a late correction mechanism). However, these participants were less accurate in the mostly alcohol block, suggesting they still experienced conflict here and were unable to effectively utilise proactive control to cope with this more frequent conflict. Therefore, it is suggested that individual differences in alcohol sensitivity may contribute to the effective use of proactive control, particularly in the presence of alcohol-related stimuli.

1.11.6 Working Memory

In addition, there is also a possibility that individual differences in Working Memory Capacity (WMC) may explain differences in the ability to utilise proactive control (Braver, 2012). This is because WMC is thought to be essential to guide future behaviour and therefore individuals with a high WMC may have an increased ability to actively maintain a goal (Braver, 2012; Redick, 2014; Richmond et al., 2015). Indeed, research has implied that WMC predicts performance in various cognitive tasks (Richmond et al., 2015). Importantly, some research (e.g. (Redick & Engle, 2011; Wiemers & Redick, 2018)) has showed that performance on the AX-Continuous Performance Test (Lesh et al., 2013) is affected by WMC i.e. those with a high-WMC tend to perform better than those with a low-WMC. During this task, participants are required to make a target response when presented with a specific sequence of stimuli (usually letters e.g. an A followed by an X) and a non-target response when other sequences are presented (e.g. an A followed by a Y). Importantly, the target sequence is presented frequently to build a pre-potent response and therefore response inhibition is required when other sequences are presented. This task (or variations) have been regularly used as a measure of proactive and reactive control (e.g. (Gonthier, Macnamara, Chow, Conway, & Braver, 2016) see chapter three for more information on this task).

Other research has also supported this (e.g. (Richmond et al., 2015; Wiemers & Redick, 2018) demonstrating that those with a high-WMC tend to be more proactive than those with a lower-WMC, who tend to rely more on reactive control as a late correction mechanism. Certainly, Finn et al (Finn, Justus, Mazas, & Steinmetz, 1999) also demonstrated that individual differences in WMC mediated the effect of acute alcohol intoxication on inhibitory control. However, this study only focused on 'reactive' inhibitory control and therefore there is still a lack of knowledge concerning which sub-processes (if any) of inhibitory control are modulated by WMC. Further research investigating the relationship between inhibitory control processes and WMC could have useful implications for understanding Substance Use Disorders, as there is consistent evidence that both heavy drinking individuals and individuals with a Substance Use Disorder display deficits in Working Memory tasks (e.g. (Bechara & Martin, 2004; Mahedy et al., 2018; Noël et al., 2001).

1.12 Interim summary

To summarise so far, inhibitory control is typically investigated as a reactive stopping response in the addiction literature, despite neurocognitive models (Verbruggen, McLaren, et al., 2014) suggesting this is an *over-simplistic* conceptualisation. Therefore, the primary aim of this thesis was to break down the homunculus by examining both reactive and proactive control in heavy drinkers. Secondly, the mechanisms underlying the preparation of responses in heavy drinkers are also poorly understood. Therefore, I also aimed to investigate two potential mechanisms (Working Memory Capacity and alcohol sensitivity) that may underlie effective use of proactive control. Following on from this, the second primary focus of this thesis was to investigate the stability of these inhibitory control processes, discussed below.

1.13 Inhibition as a transient variable

Although much research has recognised inhibitory control as a risk factor for Alcohol Use Disorders, these studies do not explain whether or not the ability to inhibit inappropriate behaviour is stable over extended periods *within* individuals. Indeed, there is strong evidence to suggest that inhibitory control may be subject to short-term fluctuations *within* individuals (de Wit, 2009; Jones, Christiansen, et al., 2013), suggesting that the capacity to proactively prepare, choose and stop a response is fluid. These fluctuations can occur in response to physiological, environmental or psychological triggers (de Wit, 2009; Jones, Christiansen, et al., 2013) such as alcohol intoxication, substance-cue exposure, and acute stress, all of which are further described below. Indeed, de Wit (de Wit, 2009) suggests that these short-term fluctuations may be especially detrimental to abstainers as a short-lived lapse of control could lead to a relapse of substance use. However, in relation to the first focus of this thesis, these theories of fluctuating disinhibition are based on an *over-simplistic* view of inhibitory control i.e. inhibitory control as a reactive stopping response. As a result, a second key aim of this thesis was to explore if some of the environmental and psychological mechanisms suggested (alcohol intoxication, alcohol-cue exposure, acute stress) lead to short-term fluctuations in both reactive and proactive control, and if these impairments are related to increased alcohol consumption.

1.13.1 The pharmacological effects of alcohol

There is considerable evidence that acute alcohol intoxication increases both subjective (e.g. self-reported craving) and objective (e.g. bogus taste test) measures of subsequent alcohol seeking in both alcohol dependent patients and healthy social drinkers (de Wit & Chutuape, 1993; Fernie, Christiansen, Cole, Rose, & Field, 2012; Rose & Grunsell, 2008). However, the mechanisms through which this effect occurs are still open to debate (Field, Wiers, Christiansen, Fillmore, & Verster, 2010). Indeed, it is well reported that alcohol intoxication has a detrimental effect on executive and psychomotor functions such as working memory, planning and inhibitory control (e.g. (Christiansen, Rose, Cole, & Field, 2013; Marczinski, Abroms, Van Selst, & Fillmore, 2005; Weissenborn & Duka, 2003)).

Specifically, there is an extensive body of evidence which has reported that inhibitory control is impaired by both moderate (0.4g/kg) and high doses (0.8g/kg) of alcohol (Abroms & Fillmore, 2004; de Wit, Crean, & Richards, 2000; Fillmore, Ostling, Martin, & Kelly, 2009; Marczinski et al., 2005; Weafer & Fillmore, 2008). Indeed, impairments in inhibitory control have been reported following alcohol doses that are not large enough to effect general psychomotor functions, perhaps suggesting unique impairing effects of alcohol intoxication on inhibitory control ((Fillmore, 2003) see also (Fillmore, 2007)). This is supported by a recent systematic review (Weafer & Fillmore, 2016) which concluded that alcohol priming reliably impairs inhibitory control, at doses which are below the legal driving limit in the USA (80mg/100ml). These doses also lead to increased risk-taking behaviour, though delay discounting was not impaired; with studies investigating this having produced contradictory findings (e.g. (Ortner, MacDonald, & Olmstead, 2003; Reynolds, Richards, et al., 2006; Richards, Zhang, Mitchell, & de Wit, 1999)).

Consequently, the large body of evidence demonstrating that alcohol intoxication impairs inhibitory control has led to a suggestion that the alcohol priming effect may be mediated by impairments in inhibitory control (Field et al., 2010; Jones, Christiansen, et al., 2013). Indeed, one study (Weafer & Fillmore, 2008) demonstrated that a 0.65g/kg alcohol dose impaired performance on a Go/No-go task and that individual differences in the degree of impairment from alcohol intoxication were positively associated with *ad-libitum* alcohol consumption. However, as Knibb et al (Knibb, Roberts, Robinson, Rose, & Christiansen, 2018) note, this study fails to provide strong evidence that inhibitory control impairments mediate the alcohol priming effect, as alcohol-seeking was measured in a separate testing session to consumption of the priming drink. Therefore, inhibition was not required during the *ad libitum* taste test session. As a result, it is hard to argue that the alcohol priming effect

is the result of a failure of inhibitory control from this study. To my knowledge, no evidence that measures alcohol-seeking in the same session as consumption of the alcohol prime, demonstrated that inhibitory control impairments mediate the alcohol priming effect (e.g. (Christiansen et al., 2013; Fernie et al., 2012)).

Therefore, it is still unclear whether temporary impairments in inhibitory control mediate the alcohol priming effect. Furthermore, to my knowledge only one study has investigated the effect of alcohol priming on proactive control. In this study (Campbell et al., 2017), alcohol intoxication led to impairments in 'reactive' motor (but not saccadic) inhibitory control but did not significantly impair proactive control. However, it is not possible to make robust conclusions regarding this due to a paucity of literature. By developing this line of research, we may increase understanding of which inhibitory control processes (if any) mediate the alcohol priming effect.

1.13.2 The anticipated effects of alcohol

Research has also demonstrated that consumption of a placebo-alcohol increases subsequent subjective (e.g. self-reported craving) and objective (e.g. bogus taste test) measures of alcohol seeking (Christiansen, Jennings, & Rose, 2016; Christiansen et al., 2013; Christiansen, Townsend, Knibb, & Field, 2017; Rose, Hobbs, & Drummond, 2013). One study (Leeman, Corbin, & Fromme, 2009) also showed that *ad libitum* alcohol consumption was predicted by self-reported craving after consumption of a placebo-alcohol drink. However, this was not the case following consumption of an alcoholic drink. These studies therefore imply that increases in self-reported craving and alcohol-seeking following an alcoholic priming drink are at least partially the result of the anticipated effects of alcohol, and not solely the pharmacological effects (Christiansen et al., 2017).

Regardless, only a small number of studies have investigated the effects of a placebo on executive functions such as inhibitory control. For example, Christiansen et al (Christiansen et al., 2016) found that the consumption of a placebo-alcohol prime lead to increased craving and deficits in inhibitory control compared to a control prime. Furthermore, Christiansen et al (Christiansen et al., 2013) tested participants during three sessions (alcohol, control, placebo). They demonstrated that although craving was increased by both the alcohol and placebo drink compared to the control, only the alcoholic drink impaired executive functions and increased alcohol seeking compared to the placebo and control primes. There was no difference in these measures following the placebo-alcohol and

control primes. Consequently, the authors suggested that those studies which compare the effects of a placebo-alcohol to alcohol (and not a control that participants are told does not contain alcohol) are failing to recognize that outside of the laboratory, both the anticipated and pharmacological effects of alcohol contribute to the alcohol priming effect and the impairing effect of alcohol on cognitive functions. Indeed, the common methodology of priming studies follows the procedure of comparing alcohol effects to placebo effects. It is only with more studies including a control session, can we fully understand the effects of alcohol on inhibitory control.

Lastly, the small number of studies which have investigated the effect of an alcohol-placebo on inhibitory control have focused only on 'reactive' inhibitory control. There have been no studies which have investigated the effect of a placebo-alcohol on the other inhibitory processes (e.g. signal detection, proactive control). Therefore further research is necessary to disentangle the anticipated and pharmacological effects of alcohol on inhibitory control processes.

1.13.3 Alcohol Cue reactivity

Furthermore, it is well recognised that exposure to substance-related cues (e.g. the smell or sight of beer) leads to increases in craving, physiological responses (such as increased heart rate or salivation (e.g. (Pomerleau, Fertig, Baker, & Cooney, 1983)) and behavioural responses (such as increased use of the substance in substance users (e.g. (Carter & Tiffany, 1999; Veilleux & Skinner, 2015)). This is referred to as 'cue reactivity' and is thought to contribute to the transition to substance dependence (Drobes, 2002) and relapse (Goldstein & Volkow, 2002; Stacy & Wiers, 2010). Alcohol-cue exposure has also been shown to increase alcohol seeking in non-dependent samples (Christiansen et al., 2017; Jones, Rose, Cole, & Field, 2013; MacKillop & Lisman, 2007), although, differences between these samples have also been reported. For example, one study (Thomas, Drobes, & Deas, 2005) reported that adolescents with a substance dependence showed increased salivation when exposed to substance cues compared to non-dependent adolescents. However, there was no difference in heart rates during exposure.

As such, there is a general consensus that associative learning mechanisms play a key role in the above responses to substance-cues (Field & Jones, 2017). Indeed, Incentive-Sensitization theories (Robinson & Berridge, 1993) argue that individuals build associations between the substance-related cues and the positive effects of the substance. Therefore, these

cues become more salient to the substance user and promote drug-seeking and consumption. Evidence supporting this theory suggests that substance-related cues lead to increases in dopamine release (Boileau et al., 2007; Koob & Volkow, 2010), although other evidence has showed lower dopamine release or receptors in those with a substance addiction (Martinez et al., 2004; Martinez et al., 2007; Volkow et al., 1990). Support for this has also been found using Ecological Momentary Assessment (EMA) methods which have demonstrated that substance-cue exposure increases craving and substance use in naturalistic environments (e.g. (Fatseas et al., 2015; Serre, Fatseas, Swendsen, & Auriacombe, 2015)).

Despite this, there is some disagreement about other psychological mechanisms that may explain this relationship (Field & Jones, 2017). Much evidence has investigated inhibitory control as a possible mechanism involved. For example, one study (Papachristou, Nederkoorn, Havermans, van der Horst, & Jansen, 2012) reported that inhibitory control moderated the relationship between alcohol-cue exposure and increased craving in heavy drinkers. Specifically, following alcohol-cue exposure, those with poorer response inhibition reported increased alcohol craving compared to those with better response inhibition. However, despite also showing increased craving following cue-exposure, inhibitory control did not moderate this relationship in light drinkers. Importantly, Field and Jones (Field & Jones, 2017) also reported that increases in disinhibition and craving in non-dependent drinkers partially mediated the effect of alcohol-cue exposure on alcohol consumption during a bogus taste test.

Other evidence has demonstrated that alcohol-cue exposure impairs inhibitory control in alcohol dependent patients (e.g. (Gauggel et al., 2010; Noël et al., 2007)), however, another study (Mainz et al., 2012) reported no differences in response inhibition in male dependent drinkers following alcohol-cue exposure (compared to neutral). There are also some discrepancies in non-dependent drinkers. For example, some research using alcohol cues embedded into Stop-Signal and Go/No-go tasks have demonstrated short-term deficits in inhibitory control (Muraven & Shmueli, 2006; Petit, Kornreich, Noël, Verbanck, & Campanella, 2012), including both problem and non-problem non-dependent drinkers (Kreusch, Vilenne, & Quartemont, 2013). ERP research has also demonstrated decreased N200 components following alcohol-cue exposure (compared to neutral cue-exposure) in non-dependent drinkers, or differences in N200 amplitudes between heavy drinkers compared to light drinkers in response to alcohol-cues (Kreusch, Quertemont, Vilenne, & Hansenne, 2014; Watson, Newton-Mora, & Pirkle, 2016). However, other research has failed to demonstrate this. For example, one study (Nederkoorn et al., 2009) reported no impairments

in inhibitory control following alcohol-cue exposure (through images) in non-dependent social drinkers. Similarly, Jones et al (Jones, Rose, et al., 2013) found no impairments in inhibitory control when a sample of non-dependent drinkers smelt and held an alcoholic drink compared to a control.

As such, a recent meta-analysis (Jones, Robinson, et al., 2018) reported that the effect of alcohol-cue exposure on inhibition was indeed small (Standardised mean difference = -0.21, 95% CI = −0.32, −0.11) but also robust across Stop-Signal, Anti-Saccade and Stroop tasks. Therefore, it is possible that the increased alcohol-seeking demonstrated following alcohol-cue exposure may be the result of short-term fluctuations in inhibitory control. These fluctuations may prevent individuals from being able to self-regulate their behaviour in response to the temptation for alcohol and therefore lead to an increase in alcohol-seeking or consumption (de Wit, 2009; Jones, Christiansen, et al., 2013). It should also be noted that there is a suggestion that alcohol-cue exposure may intensify the impairments in inhibitory control following alcohol intoxication (e.g. (Adams, Ataya, Attwood, & Munafo, 2013; Weafer & Fillmore, 2015)). This may be because of increased salience to these cues during intoxication (Field et al., 2010), although see (Duka & Townshend, 2004) who only found increased attentional bias to alcohol-cues during a low alcohol dose (0.3g/kg). Nonetheless, this exacerbation in deficits experienced when presented with alcohol-cues during intoxication may further contribute to a "loss of control" over drinking (Weafer & Fillmore, 2015).

However, the research described above only investigated 'reactive' inhibitory control which may contribute to the discrepancies in findings. Research suggests that alcohol-cue exposure may induce cognitive biases, that influence proactive slowing and the execution of reactive stopping (Stacy & Wiers, 2010). Indeed, research by Sharma (Sharma, 2017) demonstrated how alcohol-cue exposure (compared to neutral-cue exposure) had detrimental effects on the performance of heavy drinkers (compared to light drinkers) in a modified Stroop task. The performance of these individuals suggested that heavy drinkers were relying on reactive control to act as a late correction mechanism (see also (Braver, 2012)), whereas the lighter drinkers were utilising proactive control to filter out the context of the prior cues. Other substances have also been investigated, for example Brevers et al (Brevers et al., 2017) found that participants with a Cannabis Use Disorder (who were pursuing treatment) had poorer proactive and reactive inhibition compared to healthy controls. However, the cannabis users did demonstrate increased proactive control when presented with cannabis-related cues in comparison to neutral-related cues; but this was likely due to their motivation to cut

down/quit. Consequently, further research is required to investigate the effect of alcohol-related cues on proactive control, and whether impairments in inhibitory processes following alcohol-cue exposure lead to subsequent alcohol-seeking.

1.13.4 Stress

Lastly, emotional stress is also thought to be a risk factor for substance use and relapse (see (Sinha, 2001) for a review). In support of this, experimental research has demonstrated that acute stress increases craving for alcohol (Field & Powell, 2007), various measures of the personal value of alcohol (Owens, Ray, & MacKillop, 2015) and *ad libitum* alcohol consumption in heavy drinkers (McGrath, Jones, & Field, 2016). Other research has demonstrated that social drinkers will readily consume more alcohol following stress (de Wit, Soderpalm, Nikolayev, & Young, 2003; Magrys & Olmstead, 2015), although it should be noted that the self-reported measure of stress was unrelated to *ad libitum* alcohol intake in one of these studies (Magrys & Olmstead, 2015). Similar evidence has been reported in substance dependent individuals. For example, Thomas et al (Thomas, Bacon, Randall, Brady, & See, 2011) demonstrated that non-treatment seeking alcohol dependent individuals are more likely to consume all of an *ad libitum* alcohol beverage following stress. Longitudinal evidence has also supported a causal relationship between stress and alcohol use (Boden, Fergusson, & Horwood, 2014; Russell, Cooper, Frone, & Peirce, 1999), and a literature review (Enoch, 2011) stated that there is causal relationship between exposure to chronic stress during childhood and developing a Substance Use Disorder during early adulthood. Enoch (Enoch, 2011) suggests that this process develops through a transition from heavy drinking during adolescence; however this pathway can be enhanced or nullified due to the influence of the individual's surroundings and genes.

Despite this seemingly robust evidence for a causal relationship between stress and increased alcohol use, it is unclear which psychological mechanism(s) underlie this relationship (McGrath et al., 2016). In a review of the literature, Jones et al (Jones, Christiansen, et al., 2013) suggest that stress may be another psychological trigger which leads to short-term fluctuations in inhibitory control *within* individuals. Certainly, it has been suggested that the same neural systems (specifically activity in the PFC) control the emotional regulation of stress and inhibition of incongruous behaviour (Li & Sinha, 2008). Therefore, it is possible that the control of behaviour is interrupted during or following experiences of stress which may lead to increased drug seeking (Sinha, 2001). Supporting

evidence for this has revealed that stress is related to impairments in the PFC (see (Hermans, Henckens, Joels, & Fernandez, 2014) for a review), and this area of the brain is seemingly the most vulnerable, such that even mild exposure to stress can cause dramatic impairments (Arnsten, 2009).

However, research investigating the effect of acute stress on inhibitory control has reported contradictory results. For example, acute stress has been shown to impair inhibitory control in healthy participants (Scholz et al., 2009; Starcke, Wiesen, Trotzke, & Brand, 2016) and male problem drinkers following exposure to alcohol-related cues (Zack et al., 2011). Roos et al (Roos et al., 2017) also reported that undergraduate students in a control group had lower SSRTs in a Stop-Signal task at post-manipulation compared to pre-manipulation indicating the presence of practise effects. However, the participants in the stress group did not show this improvement in performance leading the authors to suggest that acute stress had a detrimental effect on inhibitory control. However, McGrath et al (McGrath et al., 2016) reported no effect on performance in a Stop-Signal task in heavy drinkers. Interestingly, there are studies which have reported that acute stress enhanced the performance of opiate users and controls on a Go/No-go task (Constantinou et al., 2010) and healthy participants on a Stop-Signal task (Schwabe, Hoffken, Tegenthoff, & Wolf, 2013). Therefore, it could be that the effect of stress on inhibitory control is in accordance with a U-shaped function (Jones, Christiansen, et al., 2013). Indeed, in two experiments using a Stroop task, Henderson et al (Henderson, Snyder, Gupta, & Banich, 2012) reported that exposure to a moderate level of stress was associated with improved performance, whereas exposure to a low or high level of stress was associated with poorer performance. Therefore, further research is required to expand our understanding of the effect of acute stress on reactive control and there is no research to my knowledge, which investigates the effect of acute stress on proactive control.

To summarise, research has suggested that impairments in inhibitory control are subject to fluctuations *within* individuals following exposure to various psychological processes or environmental triggers. These fluctuations in the ability to inhibit behaviour are suggested to play a causal role in alcohol seeking and relapse. In addition to those described above, there are other environmental and psychological triggers (e.g. arousal and emotional states, ego depletion, beliefs), which are suggested to cause fluctuations in inhibitory control *within* individuals (Jones, Christiansen, et al., 2013). However, there is less research investigating the effects of these on inhibition and alcohol-seeking. As a result, I opted to focus the research in this thesis on the effect of alcohol intoxication, alcohol-cue exposure and acute stress on inhibitory control processes.

1.14 Summary of Aims and Hypotheses

The overall aim of this thesis was to investigate the relationship between reactive and proactive inhibitory control processes and alcohol use in non-dependent, heavy drinkers. Specifically, to investigate whether exposure to environmental and psychological triggers (alcohol intoxication, alcohol-cue exposure and exposure to acute stress) lead to short-term impairments in reactive and proactive inhibitory control, and whether these impairments were related to increased alcohol-seeking. This was based on evidence from Verbruggen et al (Verbruggen, McLaren, et al., 2014) who suggest that there is an *over-simplistic* conceptualisation of inhibitory control as a reactive stopping response in the literature. I also based our aims and hypotheses on evidence from two literature reviews (de Wit, 2009; Jones, Christiansen, et al., 2013) that suggest inhibitory control fluctuates *within* individuals when presented with environmental and psychological triggers (e.g. alcohol intoxication, alcohol-cues, and acute stress). Therefore, I aimed to specify which inhibitory processes (if any) are impaired by these triggers, and which of these processes (if any) predict increased alcohol seeking. This research could potentially contribute to the development of addiction interventions that centre around improving reactive or proactive control and protecting individuals from temporary fluctuations in these processes. Throughout these studies, I recruited heavy drinkers and excluded individuals who self-reported a previous or current diagnosis of alcohol dependency or had received treatment. This was partly due to ethical constraints, but also to allow an investigation into individuals who are at risk of developing an alcohol dependence. Lastly, I also investigated potential mediators of the relationship between inhibitory control processes and alcohol seeking. These included measures of poor Working Memory Capacity and low alcohol sensitivity, both of which have been related to increased alcohol consumption.

In chapter three, I focused on isolating reactive control and proactive slowing in heavy drinkers to support the notion that a focus only on reactive stopping is over-simplistic, and to identify a task which I could use moving forward in my research. I also investigated whether individual differences in these processes were associated with individual differences in self-reported alcohol consumption. In chapter four, I used a modified Stop-Signal task from chapter three to investigate whether reactive stopping, proactive slowing and signal detection were impaired by exposure to alcohol-related cues (study two) and alcohol priming (study three). I also investigated whether alcohol seeking increased following cue-exposure

and priming, and whether individual differences in the inhibitory processes predicted individual differences in *ad libitum* alcohol consumption.

Chapter five sought to investigate the relationship between inhibitory control processes and alcohol consumption, in the presence of alcohol-related cues, outside of the laboratory using two online studies. I also aimed to investigate potential mediators of these relationships, including Working Memory Capacity and low alcohol sensitivity.

Chapter six then sought to provide neuropsychological evidence. I aimed to investigate the effect of acute stress on inhibitory processes, and the neurological correlates of inhibitory control, in the presence of alcohol-cues. I also aimed to investigate whether exposure to a psychosocial stressor increased alcohol seeking, and whether the magnitude of impairments in behavioural inhibition and the neurological responses to alcohol-related cues, predicted increased alcohol consumption. Lastly, I aimed to investigate whether individual differences in alcohol sensitivity and Working Memory Capacity were associated with *ad libitum* alcohol consumption, and the behavioural and neurological correlates of inhibitory control.

Chapter 2

General Methods and Materials

2.1 Self-report measures

At the start of each laboratory study (studies one, two, three and six), participants were required to fill in various baseline measures to assess their personality and alcohol consumption. During the online studies (studies four and five), participants were only required to complete baselines measures of alcohol consumption. All of these measures are described in detail below. Following this, is a description of the Subjective Intoxication Scale which was distributed in study three, and the *Ad libitum* taste test which was used in studies two, three and six. The Alcohol sensitivity questionnaire is also described which was distributed in studies five and six, as is the State Trait Anxiety Inventory which was distributed in study six. Lastly, participants also filled in a funnelled debriefing at the end of each laboratory study which was mostly consistent across studies. This is also described below.

2.1.2 The Alcohol Use Disorders Identification Test (AUDIT: (Saunders, Aasland, Babor, De la Fuente, & Grant, 1993))

The AUDIT questionnaire (see Appendices 1.A) was administered to participants to measure hazardous drinking. This was originally developed to screen for alcohol misuse and dependence so that individuals who would benefit from cutting down or abstaining from drinking could be quickly identified (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001). This questionnaire includes 10 fixed-response items with varying answers. The first three questions measure the frequency and quantity of alcohol consumption (for example, "*How often do you have a drink containing alcohol?").* Often these three questions are used in a short from of the AUDIT, known as the AUDIT-C. However, in these studies the full version was administered. Question 4 to 10 relate to behaviours and consequences that may or may not have occurred following alcohol consumption (for example, "*Have you or someone else been injured because of your drinking?*") The 10 items give an overall score between 0 and 40 with higher scores indicating greater alcohol consumption. Specifically, the WHO suggest that a score between 0 and 7 implies a low risk of alcohol problems, a score between 8 and 15 indicates an increased risk (or medium level) of hazardous drinking, a score between 16 and

19 suggests a higher risk of alcohol problems and a score over 20 is thought to suggest probable alcohol dependence (Babor et al., 2001). Furthermore, the WHO suggests that simple or brief feedback and advice on drinking would be the most appropriate intervention for an individual who scores between 8 and 15. However, if an individual's score is between 16 and 19 it would be more appropriate to suggest that the individual seeks some counselling advice, and a score above 20 indicates the need for a referral to further alcohol harm assessment to evaluate a diagnosis of alcohol dependence (Babor et al., 2001).

As a one-factor measure, the AUDIT has been shown to have good internal consistency in both non-clinical (Cronbach's $\alpha = .82$) and clinical samples (Cronbach's $\alpha = .88$) (Shields, Guttmannova, & Caruso, 2004). The test-retest reliability has also been reported as generally good in general population samples (Dybek et al., 2006). Other research has demonstrated that the AUDIT is a valid and a sensitive screening method to recognise hazardous drinkers and those with an Alcohol Use Disorder in the general population (intra-class correlation coefficient for the total score =.95) (Dybek et al., 2006). Therefore, the AUDIT is thought to be a useful measure of hazardous drinking and potential alcohol dependence.

2.1.3 The Timeline Follow-Back (TLFB: (Sobell & Sobell, 1990))

Participants were also asked to fill in a TLFB (see Appendices 1.B) to measure retrospective alcohol consumption in units (one UK unit = 8 g of alcohol). Participants were asked to fill in the number of units they consumed on a day-to-day basis for the previous 7 (study four) or 14 days (studies one to three, five to six) up until the day before the study took place. Participants were able to use their diaries or mobile phones to remind them of their consumption and a guide providing the number of units in standard UK drinks (e.g. A 330ml bottle of beer or cider, 5% ABV is 1.7 UK Units or 25ml (a single measure) of spirit 40% ABV is 1 UK Unit) was also provided to assist participants in calculating their alcohol consumption.

The TLFB can also be administered for specific periods up to 12 months (e.g. 30 days), however research has shown discrepancies in accuracy for longer lengths of recall (e.g. (Hoeppner, Stout, Jackson, & Barnett, 2010)). Indeed, this study found that social drinkers reported an increased number of total drinks, an increased number of days with consumption of 4 or more drinks and less abstinent days in repeated one-week TLFBs compared to a 30-day TLFB. However, other research has demonstrated good test-retest reliability when

comparing a 30-day to a 90-day TLFB in psychiatric outpatients (r's > .73) (Carey, Carey, Maisto, & Henson, 2004). High test-retest reliability has been demonstrated in social drinkers between telephone and online administration (r's > .75) (Rueger, Trela, Palmeri, & C King, 2012) and problem drinkers when comparing standard paper-and-pencil method to versions on a computer (Pearson r correlation coefficients > .83), or when comparing administration on the telephone to the standard self-administered method (r's > .77) (Sobell, Brown, Leo, & Sobell, 1996). This is also acceptable when gathering data on self-reported smoking (r's > .75), cocaine (r's > .65) and cannabis (r's > .70) (Robinson, Sobell, Sobell, & Leo, 2014). Therefore, the TLFB is considered to a reliable and useful measure of alcohol consumption with psychometrically sound properties.

2.1.4 The Brief Comprehensive Effects Of Alcohol Questionnaire (B-CEOA: (Ham, Stewart, Norton, & Hope, 2005))

The B-CEOA (see Appendices 1.C) consists of 15 items, which measure alcohol outcome expectancies (what individuals expect to happen when they have consumed alcohol) and evaluations of these expectancies. These items are measured using a four-point Likert scale between strongly disagree to strongly agree. The questionnaire measures both positive expectancies (Tension reduction; Social facilitation; Liquid courage; Self perception) and negative expectancies (Cognitive-behavioural impairment; Risk taking/aggression; Negative self-evaluation). Participants first indicate how likely a specific effect will occur from drinking alcohol (e.g. 'When I drink alcohol I would feel dizzy') on 15 items, measured from 1 ('disagree') to 4 ('agree'). Respondents also indicate to what degree each specific effect would be desirable or adverse, measured from 1 ('bad') to 5 ('good') (Ham, Wang, Kim, & Zamboanga, 2013).

This questionnaire is a short version of the original Comprehensive Effects of Alcohol Questionnaire (Fromme, Stroot, & Kaplan, 1993). The items included here were extracted from the original questionnaire, with eight items extracted from the positive expectancy factor and seven from the negative expectancy factor. The internal consistency of the brief measure has been shown to replicate the original version in university students with alpha's ranging from .60 to .81. The concurrent validity is also similar to the original version in this study (Ham et al., 2005). Other studies have supported this in students demonstrating Cronbach's alpha's of .85 to .90 (Hatzenbuehler, Corbin, & Fromme, 2008) and .77 to .83 (Zamboanga et al., 2012). Lastly, Ham et al (Ham et al., 2013) also found support for the use

of these subscales in university students across genders and different ethnicities. Specifically, the factor structure and the associations between these subscales and hazardous drinking were similar across genders and individuals with various ethnic backgrounds, suggesting this is a reliable measure of alcohol outcome expectancies.

2.1.5 The Temptation Restraint Inventory (TRI: (Collins & Lapp, 1992))

The TRI (see Appendices 1.D) was distributed to measure drinking restraint (preoccupation with and efforts to reduce drinking). This consists of 15 items which focus on how often individuals think about or attempt to manage their alcohol consumption. Each item is scored on a 9-point Likert scale from 1 (not at all or never) to 9 (extremely or always). These 15 items comprise five factors; Govern, Emotion, Restrict, Concern about drinking and Cognitive Preoccupation, which have demonstrated good internal reliability (e.g. (Collins, George, & Lapp, 1989) α = 0.76 to 0.91). In addition, these five factors comprise two higher order factors known as Cognitive Behavioural Control (CBC) which measures drinking control and Cognitive Emotion Preoccupation (CEP) which measures temptation to consume alcohol (Lyvers, Hasking, Hani, Rhodes, & Trew, 2010).

The use of this two-factor structure has been supported in undergraduate samples. For example, MacKillop et al (MacKillop, Lisman, & Weinstein, 2006) reported good overall internal consistency *(*α = .87) for hazardous and harmful drinkers. Specifically, each higher-order factor *(*CEP α= .85; CBC α = .80) also had high internal reliability for both hazardous drinking and harmful drinking groups. Other studies (e.g. (Collins, Koutsky, & Izzo, 2000) using social drinkers have also demonstrated good internal reliability (CEP α= .91; CBC α= .79), as well as good discriminant and convergent validity. Therefore, the TRI is suggested to have sound psychometric properties and is a reliable measure of drinking restraint.

2.1.6 The Barratt Impulsivity Scale (BIS: (Patton et al., 1995))

The BIS (see Appendices 1.E) was administered to measure self-reported trait impulsivity across three dimensions (Motor, Non-Planning and Attentional). This consists of 30 items, each scored from 1-4 (rarely, occasionally, often and always). A total score can be calculated for each of the three subscales; however, it is also possible to compute an overall measure of impulsivity (usually referred to as BIS Total Score) by adding together the total scores on all three subscales. Higher scores indicate increased impulsivity in each dimension, but also overall. Indeed, this scale is one of the most frequent measures of impulsivity in both clinical

and research environments (Stanford et al., 2009). This study demonstrated moderate-high internal reliability and test-retest reliability on total scores of the BIS (α = .83; r_s = .83) and the Attentional (α =.74; r_s =.61), Motor (α =.59; r_s = .67) and Non-Planning (α = .72; r_s= .72) dimensions, in a combined sample of both college students and healthy adults.

2.1.7 The Approach and Avoidance of Alcohol Questionnaire (AAAQ: (McEvoy, Stritzke, French, Lang, & Ketterman, 2004))

The AAAQ- right now version (see Appendices 1.F) was used to measure the motivation of participants to approach and avoid drinking alcohol in the current moment. This scale consists of 14 items scored from 0 (not at all) to 8 (very strong) to measure three sub-scales of craving; mild inclinations to drink (Inclined-Indulgent), intense inclinations to drink (Obsessed-Compelled) and inclinations to avoid alcohol (Resolved-Regulated). These subscales have showed good internal reliability in heavy drinkers (e.g. (Field & Jones, 2017) Inclined-Indulgent (α = .87), Obsessed-Compelled (α = .83) and Resolved-Regulated (α = .73)) and alcohol dependent inpatients (e.g. (Field, Di Lemma, Christiansen, & Dickson, 2017), Inclined-Indulgent (α = .77), Obsessed-Compelled (α = .72) and Resolved-Regulated (α = .82)). Another study (Klein & Anker, 2013) provided similar reliability estimates in alcohol dependent patients (14 items α = .71), showing the Obsesses-Compelled subscale to have the highest reliability (α = .90), followed by the Inclined-Indulgent (α= .87) and the Resolved-Regulated (α= .75). The convergent validity and predictive validity in this study also suggested that the AAAQ was a psychometrically sound measure of alcohol craving.

Brief Mood Introspection Scale (BMIS: ((Mayer & Gaschke, 1988))

The BMIS (Appendices 1.G) was also administered in study one as part of the baseline measures. This contains sixteen adjectives of feelings (e.g. Lively, Sad, Tired, Grouchy) and participants are required to indicate how these describe their present mood on a four-point scale (‘*definitely do not feel,’ ‘do not feel,’ ‘slightly feel’ or ‘definitely feel’*). These individual adjectives are then loaded onto four factors; Arousal-Calm, Negative-Relaxed, Pleasant-Unpleasant and Positive-Tired. This has been used in previous research in similar samples to those recruited in the research for this thesis (e.g. (Field & Jones, 2017; Jones, Field, et al., 2013)). The four factors of the scale have been found to be reliable (Mayer, Allen, & Beauregard, 1995) with Cronbach’s alphas generally ranging from 0.76 to 0.83,

although some slightly lower have been reported e.g. 0.60 to 0.80 (Kokkonen & Pulkkinen, 2001).

2.1.8 The Subjective Intoxication Scales (SIS: (Duka, Tasker, & Stephens, 1998))

The SIS (see Appendices 1.H) was administered in study three, following the alcohol, alcohol-placebo and control priming drinks. This was used to measure six subjective feelings, which included 'lightheaded,' 'irritable', 'stimulated', 'alert', 'relaxed' and 'contented.' These were scored using a 1-10cm Likert scale rated from 'Not at all' to 'Extremely.' This scale has demonstrated good reliability in previous studies using similar samples to the current studies (e.g. (Knibb et al., 2018) (Study 1: $\alpha = .83$, Study 2: $\alpha = .86$)).

2.1.9 *Ad libitum* taste test

In studies two, three and six, participants were required to complete an *ad libitum* taste test (see Appendices 1.I). During these, participants were presented with 250ml of chilled Skol (2.8% vol. ABV) and 250ml of chilled fresh orange juice, the volumes of which were increased to 500ml in study six. These were provided to participants in two unmarked pint glasses ensuring that participants were not aware of the brands provided. Participants were also provided with a set of 10 questions for each drink that were scored from 0 (not at all) to 10 (extremely). Using these, participants were asked to taste and score both drinks on their gustatory dimensions (e.g. *"How bitter was drink 1?" or "How light was drink 1?").* To do this, participants were also directed to '*drink as much or as little as you like in order to make accurate judgements*'. Furthermore, in order to heighten participants' motivation to control their alcohol intake, participants were also informed that alcohol may negatively impact their performance on a task to be completed after the taste test, in which they may be able to win money to add to their payment for taking part. This was based on previous studies (e.g. (Christiansen, Cole, & Field, 2012; Field & Jones, 2017)). After the experimental session concluded, the volume of the Skol lager and orange juice consumed was measured, and the amount of beer as a percentage of the total fluid consumed was calculated as the measure of *ad libitum* consumption.

The construct validity of the use of this method to measure alcohol consumption in the laboratory has been demonstrated by Jones et al (Jones, Button, et al., 2016). Through secondary analysis of 12 studies from the University of Liverpool's laboratories using a taste test (N = 762), they demonstrated that *ad libitum* alcohol consumption was significantly predicted by typical alcohol consumption measured using the TLFB ($p = .04$), craving ($p <$

.001) and pleasantness ratings of the drinks (p= .04). However, neither time of day (p= .10), day of the week (p= .14) nor awareness of the experimental aims of the taste test (p= .72) were correlated with *ad libitum* consumption. Thus, the *ad libitum* taste test is suggested to be a valid and sensitive measure of alcohol consumption in the laboratory.

2.1.10 The Alcohol-Sensitivity Questionnaire (ASQ: (Fleming et al., 2016)).

The ASQ (see Appendices 1.J) includes 15 items, which ask participants how many alcoholic drinks they must typically drink to experience alcohol-related effects. Nine of these items are associated with lower doses of alcohol and stimulation (e.g. feeling more relaxed, becoming more talkative) and six are associated with heavier doses of alcohol and sedation (e.g. passing out, throwing up). Participants are first asked whether or not they have experienced each alcohol-related effect and if the answer is YES, they are asked to estimate the minimum number of drinks required to experience the lower dose effects or the maximum number of drinks they could consume without experiencing the higher dose effects.

High scores on this questionnaire are thought to indicate low sensitivity to the sedative effects of alcohol and increased sensitivity to the stimulating effects of alcohol (Bailey & Bartholow, 2016). ASQ scores can be calculated using a standardised person mean imputation (SPMI) method (see (Lee, Bartholow, McCarthy, Pedersen, & Sher, 2015)). This helps to prevent biased low ASQ scores due to an increase in missing data in response to the items associated with the heavier doses of alcohol in comparison to the items associated with lower doses. This method involves converting each ASQ item to a z-score and then averaging across the items which are not missing to calculate a composite measure of ASQ. In healthy adults, the ASQ has demonstrated good construct validity and has reliably predicted multiple subjective effects of alcohol in a laboratory setting (Fleming et al., 2016). The internal consistency has also been shown to be excellent (α = .92) in a sample of undergraduate students (Bailey & Bartholow, 2016).

2.1.11 The State-trait Anxiety Inventory (STAI: (Spielberger, Sydeman, Owen, & Marsh, 1999))

The STAI (see Appendices 1.K) was used to measure a stress manipulation in study six. This is comprised of two subscales, each consisting of 20 items. The first subscale was administered before and after a stress manipulation to measure current feelings of anxiety, asking participants how they feel “right now” with regards to tension, worry, apprehension,

nervousness and arousal of the autonomic nervous system from “not at all” to “very much so” on a four-point Likert scale. The second subscale was administered to measure trait anxiety investigating general calmness, security and confidence from “almost never” to “almost always” on a four-point Likert scale (Julian, 2011). This inventory has been used to differentiate low and high stressful conditions (Metzger, 1976) and has been used as a measure of stress in previous studies (Field & Powell, 2007; Field & Quigley, 2009; Starcke et al., 2016). Good internal consistency has been reported in samples of students (e.g. α =0.81; (Kaupuzs, Vazne, & Usca, 2015)).

2.1.12 Funnelled debriefing

Lastly, participants also completed a short questionnaire to measure awareness of the experimental aims of each laboratory study (see Appendices 1.L). This included an open question asking what the aims of the experiment were and two fixed-response questions asking the purpose of the computer task (studies one, two, three, six) and the taste test (study two, three, six). In study six, participants were also asked what the purpose of a 5 minute presentation was.

CHAPTER 3

Isolating proactive slowing from reactive inhibitory control in heavy drinkers.

This chapter presents the first experimental chapter in this thesis, specifically a laboratory study that has been published as a brief report in Substance Use & Misuse (2019). The online supplementary materials are also presented after the article. Data is freely available on Open Science Framework (link presented in main text). The format of the original article has been modified to match the other chapters in this thesis, however the content remains the same as that of which was published. With regards to contributions, I designed the study which was approved by Andrew Jones, Paul Christiansen and Matt Field. I collected the data, analyzed this and wrote up the manuscript. Before the original submission and in response to reviewer's comments, all three co-authors provided feedback on the manuscript.

Chapter Foreword: This chapter contributed to the overall aims of this thesis by investigating whether proactive slowing could be isolated from reactive control in heavy drinkers. Importantly, this chapter also investigated whether individual differences in proactive slowing and reactive control were associated with individual differences in alcohol consumption. Lastly, this chapter utilized three inhibition tasks from the literature to ensure that they were feasible to be taken forward into the manipulation studies, particularly so that alcohol-cues could be easily embedded, and were reliable measures of response inhibition.

3.1 Abstract

Background: Impaired inhibitory control is thought to contribute to alcohol (mis)use. However, current definitions of inhibitory control are *over-simplified* by a failure to distinguish reactive inhibitory control from proactive slowing. ***Objectives:*** To distinguish 'reactive' inhibitory control and proactive slowing in heavy drinkers, and characterise associations between both constructs and individual differences in alcohol consumption. ***Methods:*** Sixty heavy drinkers completed self-reported measures of alcohol consumption, followed by two modified Stop-Signal tasks and an AX-Continuous Performance task in a laboratory setting. ***Results:*** Heavy drinkers demonstrated proactive slowing when inhibition was more likely but individual differences in proactive slowing and reactive stopping were unrelated to individual differences in alcohol consumption. ***Conclusions/Importance:*** Within a sample of heavy drinkers, individual differences in reactive inhibitory control and proactive slowing are unrelated to individual differences in alcohol consumption.

3.2 Introduction

Inhibitory control – the inability to inhibit inappropriate behaviour - is argued to play a key role in alcohol (mis)use (e.g. (de Wit, 2009; Fillmore, 2003; Goldstein & Volkow, 2002; Yucel et al., 2019)). This is often measured using the Stop-Signal or Go/No-Go task paradigms in the laboratory. During these tasks, participants are usually required to respond to go stimuli (e.g. press a key indicating the direction of an arrow (left or right)) and inhibit their response on a minority of trials when no-go stimuli or a stop-signal (e.g. the presentation of a cross) is presented (Verbruggen et al., 2019). From these, Stop-Signal Reaction Time (SSRT) - the approximate time to suppress a response following the appearance of a stop-signal (Brevers et al., 2017) - can be calculated as a covert index of inhibitory control, or the number of commission errors can be calculated as an index of inhibitory control failures.

Research utilising these tasks has demonstrated that inhibitory control deficits predict harmful drinking in non-dependent samples (Christiansen, Cole, Goudie, et al., 2012; Colder & O'Connor, 2002; Houston et al., 2014; Murphy & Garavan, 2011), as well as the progress from hazardous drinking to alcohol dependence (Rubio et al., 2008). However, there is some equivocal evidence, particularly in non-dependent samples (e.g. (Bø & Landro, 2017; Fernie et al., 2010)). One possible reason for this is that the present research focuses on reactive control processes (SSRT; 'the act of stopping'), despite cognitive neuroscience models (Verbruggen, McLaren, et al., 2014) suggesting that individuals are able to prepare inhibitory behaviour in advance and modify this 'proactively.' This may have particular relevance to substance-use behaviour (Brevers et al., 2017) as individuals often utilise proactive strategies to restrict their drinking, (i.e. preparing to have a drink-free day or to reject an offer for a drink), rather than global reactive control (i.e. inhibiting an arm movement to reach for a drink). Therefore, proactive control may offer a more informative endophenotype for substance-use behaviours (Aron, 2011).

Importantly, inhibitory control tasks can be adapted to isolate proactive control and slowing through the addition of a cue indicating stop-signal probability or a block without stop-signals (Verbruggen & Logan, 2009b). If individuals are utilising proactive control when completing the task, they should slow down their responses as stop-signal probability increases, as they prepare to inhibit their behaviour (Aron, 2011; Verbruggen, Stevens, et al., 2014). The AX- Continuous Performance Task, a modified version of the traditional Continuous Performance Test (Rosvold, Mirsky, Sarason, Bransome Jr, & Beck, 1956), has

also been used to measure reactive and proactive control (discussed below) in healthy young adults (Gonthier et al., 2016) and children (Chatham, Frank, & Munakata, 2009). During these tasks, participants are typically tasked with responding to a target stimulus or sequence (e.g. letters, numbers) and are required to withhold their response to other stimuli or sequences (Berger, Slobodin, & Cassuto, 2017).

The current study isolated 'reactive' inhibitory control and proactive slowing in heavy drinkers, and investigated whether these processes were related to individual differences in alcohol consumption. Our primary hypothesis was that individual differences in proactive slowing and reactive stopping would predict unique variance in individual differences in alcohol consumption. However, to first confirm that heavy drinkers employed proactive control strategies, we predicted that participants would: (i) slow down their responses as stop-signal probability increased in the Stop-Signal Tasks (SST) and (ii) respond to the target-response ('AX') trials faster than non-target response trials ('AY, BX, BY') in the AX-Continuous Performance Test.

3.3 Method

3.3.1 Participants

Heavy drinkers (N = 60; 40 females, mean age 22.13 ±7.99) were recruited from the University of Liverpool community, using online advertisements. The number of participants was decided upon using a power calculation to find a medium effect size ($F^2 = .20$, $\alpha = .05$, $1-\beta = 90\%$) with two predictors (reactive control, proactive slowing). Inclusion criteria included heavy drinking (defined using UK government guidelines i.e. consume > 14 UK units of alcohol per week (1 UK unit = 8g of pure alcohol)). Exclusion criteria included a self-reported previous or current diagnosis of a Substance Use Disorder, ADHD or a psychiatric disorder. The study was approved by the University of Liverpool's Research Ethics Committee. Data is freely accessible on Open Science Framework [Link: https://osf.io/p375d/].

3.3.2 Materials

Questionnaires

Participants completed a 14-day *Timeline follow back* drinking diary (TLFB: (Sobell & Sobell, 1990)), the *Alcohol Use Disorders Identification Test* (AUDIT: (Saunders et al., 1993)) (α=.69), the *Temptation and Restraint Inventory* (TRI: (Collins & Lapp, 1992)) (α's =

.51 to .75) and the *Barratt Impulsivity Scales* (BIS: (Patton et al., 1995)) (α's = .46 to .71). They also completed the 'right now' version of the *Approach and Avoidance of Alcohol Questionnaire* (AAAQ: (McEvoy et al., 2004)) (α's = .49 to .82) followed by the *Brief Mood Introspection Scale* (BMIS: (Mayer & Gaschke, 1988)) (α's =.63 to .83).

Inhibitory control tasks [1]

In the modified SST (Verbruggen, Stevens, et al., 2014), each trial began with the presentation of a white fixation line (approximately 40 mm) in the centre of the screen for 500ms. Following this, two words were presented, one immediately above and below the line. One of the words described natural objects (e.g. 'pony', 'crab') and the other described man-made objects (e.g. 'flag', 'shed'). Participants were required to respond to the position of the natural object (target) word relative to the fixation line (above or below) by a key press (no-signal trials). Words related to man-made objects were presented as distractors in the opposite location in relation to the fixation line. The task comprised two blocks (no-signal block, stop-signal block) which were completed in a counterbalanced order:

No-signal block: During this block, participants were asked to identify the position of the target word relative to the line as quickly as possible, without interruption on 100% of trials (N = 128).

*Stop-signal block***:** During this block, 75% of trials (N=96) were the same as the trials in the no-signal block as described above. The outstanding 25% of trials (N=32) were stop-signal trials in which the white fixation line in the centre of the screen increased in size by 300%. When this occurred, participants were asked to try and withhold their response. Participants were given standard Stop-Signal task instructions that sometimes this would be easy and sometimes this would be difficult or even impossible, but that they should not wait for the line to appear (Verbruggen et al., 2019).

In the Stop-signal block, we used a tracking procedure (Verbruggen & Logan, 2009a) to adjust the stop-signal delay (the delay between the presentation of the target and distractor word and the increase in size of the stop-signal) on a trial-by-trial basis. The initial stop-signal delay was 250ms, however if participants failed to withhold their response, the delay decreased by 50ms to make subsequent response inhibition easier. If participants correctly withheld their response, the delay increased by 50ms to make subsequent response inhibition more challenging. Reactive control was inferred from the mean Stop-Signal Reaction Times

[1] Task schematics are presented in the supplementary materials.

(SSRT) on no-signal trials in the stop-signal block. Proactive slowing was inferred from the degree of reaction time slowing in the stop-signal block compared to the no-signal block.

In the Stop Signal-anticipation task (SST-anticipation: (Zandbelt et al., 2011)) participants completed a single block of 342 trials. At the beginning of each trial, a horizontal line was presented at the bottom, centre and top of the screen for 500ms. The central line was assigned as the target line. Following this, a bar shaped object moved upwards at a constant speed from the bottom line to the top line. This bar reached the target response line (central line) in 800ms and the top line in 1000ms at which the trial ended. Participants were required to stop the bar as close to the target line as possible by a key press ('space bar'). These trials were no-signal trials. However, participants were also informed that on some trials the bar would stop moving automatically (stop-signal) and that they should try to withhold their response when this happened. These trials were stop-signal trials. If participants responded during a stop-signal trial or failed to respond during a no-signal trial, a red cross (+) was presented in the centre of the screen to inform participants that their response was incorrect. They were also given standard Stop-Signal task instructions as described above.

In this block, the target response line was presented in one of five different colours across trials, which was indicative of stop-signal probability. Each colour had a different stop-signal probability level; Green (0%), Yellow (17%), Orange-red (20%), Dark orange (25%) and red (33%). There were 282 no-signal trials (0% = 102; 17% = 30; 20% = 48; 25%, = 54; 33% = 48) and 60 stop-signal trials (17% = 6; 20% = 12; 25% = 18; 33% = 24). A similar tracking procedure (Zandbelt et al., 2011) was used to adjust the stop-signal delay on a trial-by-trial basis. The initial stop-signal delay was 550ms, however if participants failed to inhibit the stop-signal delay decreased by 25ms to make subsequent stopping easier. If response inhibition was successful, then the stop-signal delay increased by 25ms to make subsequent stopping harder. Reactive control was inferred from mean SSRTs on no-signal trials. Proactive slowing was indicated by the degree of slowing on trials with a 17%, 20%, 25% or 33% stop-signal probability compared to trials with a 0% stop-signal probability.

Finally in the AX-Continuous Performance Task (AX-CPT: (Lesh et al., 2013)), a white fixation cross (+) was presented in the centre of the screen for 500ms which indicated the beginning of a trial. Following this, a probe letter (A or B) was presented for 300ms followed by a target letter (X or Y) for 300ms. Participants pressed one key ('V') as quickly as possible when the 'AX' sequence was presented or a different key ('N') when other probe-target letter combinations ('AY,' 'BX,' 'BY') were presented. The maximum duration of a trial was 1500ms and correct/incorrect feedback was provided after each trial. Participants

completed one block of 120 randomised trials which consisted of 70% (N=84) of 'AX' trials in order to establish this response as dominant. The additional probe-target letter combinations comprised 10% (N=12) of trials each, based on previous research (e.g. (Redick & Engle, 2011)). Reactive inhibition was inferred from errors on AY trials. This is because these trials require the individual to override a tendency to respond to the probe letter 'A' as this is frequently followed by an 'X' target letter, which leads to a bias in responding (Paxton, Barch, Racine, & Braver, 2008; Rush, Barch, & Braver, 2006). Hence, increased errors on 'AY' trials is indicative of worse reactive control (Gonthier et al., 2016). Proactive slowing was indicated by RT slowing on 'BX' and 'BY' trials compared to 'AX' trials.

3.3.3 Procedure

Participants completed the questionnaires followed by the computerised tasks in a counterbalanced order (testing time was approximately 50 minutes). Participants were then debriefed and reimbursed through University course credit or a voucher.

3.3.4 Data reduction and analysis

One participant did not report consuming alcohol and was excluded. RTs < 100ms, > 2000ms, and outside 2.5 standard deviations from the individual's mean on the inhibitory control tasks were removed according to previous criteria (Jones & Field, 2015; Verbruggen & De Houwer, 2007). For the modified SST, data did not record for two participants and three were removed following an outlier analysis of errors. SSRTs were computed using the mean method [^{mean}RT - ^{mean}StopSignalDelay].

3.4 Results

3.4.1 Sample characteristics

Participants drank an average of 49.71 (±34.29) units in the 14 days prior to taking part and reported an average AUDIT score of 11.86 (±4.76). There were no significant differences between males (52.68 ±22.53) and females (48.30 ±38.83) in units consumed (t (57) = 0.46, p= .65, d= 0.13) or AUDIT scores (males: 11.63 ±4.84; females: 11.98 ±4.78; t (57) = -0.26, p= .80, d= 0.07). Correlations between demographic variables and inhibitory control are shown in supplementary table 1.

3.4.2 Proactive slowing across three inhibitory control tasks

In the modified SST, RTs were significantly slower in the stop-signal block (940.54 ±168.68) compared to the no-signal block (714.26 ±102.23; t (53) = -10.41, p< .001, d = 1.62) demonstrating proactive slowing.

In the SST-anticipation task, there was a significant main effect of stop-signal probability on RTs (F (1, 68) = 9.72, p= .002, η_p^2 = 0.14). Participants responded significantly faster on trials with a 0% stop-signal probability compared to trials with a 17% (p= .003), 20% (p= .002), 25% (p=.002) and 33% (p=.002) probability. Participants also responded significantly slower on 33% probability compared to 17% (p=.019), 20% (p=.022) and 25% (p=.049) probability trials. This indicates the presence of proactive slowing although there were no other significant differences (ps >.05; see table 1 for descriptive statistics).

Lastly, in the AX-CPT there was a significant main effect of trial type on RTs (F (3, 103) = 55.34, p< .001, η_p^2 = .57). Participants responded significantly slower to AY trials compared to AX trials (p< .001), BX trials (p< .001) and BY trials (p< .001) indicating proactive slowing. They also responded significantly slower to AX trials compared to BX (p=.001) and BY trials (p=. 029). There was no difference between BX and BY trials (p=.387) (see table 2 for descriptive statistics).

Table 1: Reaction times (ms) in the SST-anticipation task (N=59) split according to stop-signal probability (values are mean and SD)

	0%	17%	20%	25%	33%
RT	796.85 (112.69)	838.20 (67.95)	842.19 (74.97)	841.02 (69.47)	851.35 (87.48)

Table 2: Reaction times (ms) in the AX-CPT (N=42) split by probe-target letter combinations (values are mean and SD).

	AX	AY	BX	BY
RT	412.59 (56.53)	521.03 (90.08)	366.97 (109.55)	380.98 (125.60)

3.4.3 Prediction of alcohol consumption

Multiple regression analyses showed that the full regression models did not predict a significant amount of variance in self-reported alcohol consumption. For the modified SST (R^2 = .03; F (2, 51) = 0.80, p= .454), neither SSRTs (β= -.21, p= .212) nor proactive slowing (β= .10, p= .550) were significant predictors. Similarly, for the SST-anticipation (R^2=.02; F (2, 56) =0.57, p= .571), neither SSRT (β= -.17, p= .601) nor proactive slowing (β= -.03, p= .931) predicted alcohol consumption. Finally, for the AX-CPT (R^2= .07; F (2, 42) = 0.09, p= .912), neither reactive control (β= -.04, p= .810) nor proactive slowing (β= .05, p= .727) were significant predictors of alcohol consumption (see table 3 for descriptive statistics and correlations). [2]

3.5 Discussion

The current study demonstrated that heavy drinkers employed proactive slowing strategies when the likelihood of an inhibitory response was increased. This supports the notion that a focus only on 'reactive' control is simplistic as inhibitory control is comprised of multiple processes (Friedman & Miyake, 2004; Verbruggen, McLaren, et al., 2014) and therefore researchers should aim to be more precise when measuring and referring to inhibitory-related functions. However, individual differences in reactive stopping and proactive slowing were unrelated to individuals' alcohol consumption. This lack of significant association between reactive control and alcohol use is in contrast to previous findings (e.g. (Christiansen, Cole, Goudie, et al., 2012; Houston et al., 2014; Paz et al., 2016)). However, the evidence for this relationship is equivocal (see (Bø & Landro, 2017; Fernie et al., 2010)). Furthermore, research has demonstrated no significant differences in inhibitory control between controls and heavy drinkers (e.g. (Bednarski et al., 2012; Nederkoorn et al., 2009) or binge drinkers (e.g. (Czapla et al., 2015)). A meta-analysis also suggests impairments in non-dependent drinkers are less evident than in dependent drinkers (Smith et al., 2014).

Therefore it is possible that the relationship between inhibitory control and alcohol consumption has been overemphasized in the literature, at least in non-dependent samples. Additionally, although the null findings for proactive slowing are informative due to the paucity of literature regarding this, these must be considered in the broader context of an inconsistent relationship between reactive control and alcohol consumption. However, our

[2] TLFB data was skewed. However, log transforming this did not affect the results and therefore the non-transformed data is presented.

findings should also be interpreted in light of limitations. Certainly, the absence of a control group (e.g. light drinkers, abstainers) to compare the performance of the current sample of heavy drinkers would be a useful line of future research. Additionally, as the evidence of impairments in inhibition is more apparent in individuals who are alcohol dependent (Smith et al., 2014), it would be useful to clarify whether proactive slowing is impaired in these individuals. Finally, future research could examine the role of individual differences such as socioeconomic status, as previous research has demonstrated a direct effect on inhibitory control (Hackman, Farah, & Meaney, 2010), but also a moderating effect of the association between inhibitory control and nicotine use (Riggs & Pentz, 2016).

In conclusion, results demonstrated that heavy drinkers employed proactive slowing when the requirement for inhibition was higher. However, individual differences in proactive slowing or reactive control were not predictive of individual differences in self-reported alcohol consumption.

Table 3: Descriptive statistics and Pearson's correlations between alcohol use, reactive control and proactive control in the Stop-Signal tasks and AX-Continuous Performance Test.

	Mean (SD)	2	3	4	5	6	7
Alcohol use	49.71 (34.29)	-.15	-.01	-.14	.12	.07	.05
SSRT (Mod. SST)	391.27 (82.11)	-	.54**	-.15	.13	-.06	-.14
Proactive slowing (Mod. SST)	226.28 (159.71)		-	-.31*	.28*	-.11	-.10
SSRT (SST-antic.)	243.18 (49.52)			-	-.91**	-.04	.11
Proactive slowing (SST-antic.)	46.34 (110.04)				-	.06	-.17
Reactive control (AX-CPT)	4.22 (3.36)					-	-.01
Proactive slowing (AX-CPT)	-30.62 (84.44)						-

Reaction times are given in milliseconds. Alcohol use =alcohol units consumed in previous 14 days measured using The Timeline follow back (1 UK unit = 8g of alcohol). Mod. SST = modified Stop-Signal Task. SST-antic. = Stop Signal-anticipation task. AX-CPT = AX-Continuous Performance Task

*Correlations significant at p<. 05

**Correlations significant at p<. 01

3.6 Supplementary Information

3.6.1 Method

Inhibitory control Tasks

Fig 1. Task schematic of the modified SST.

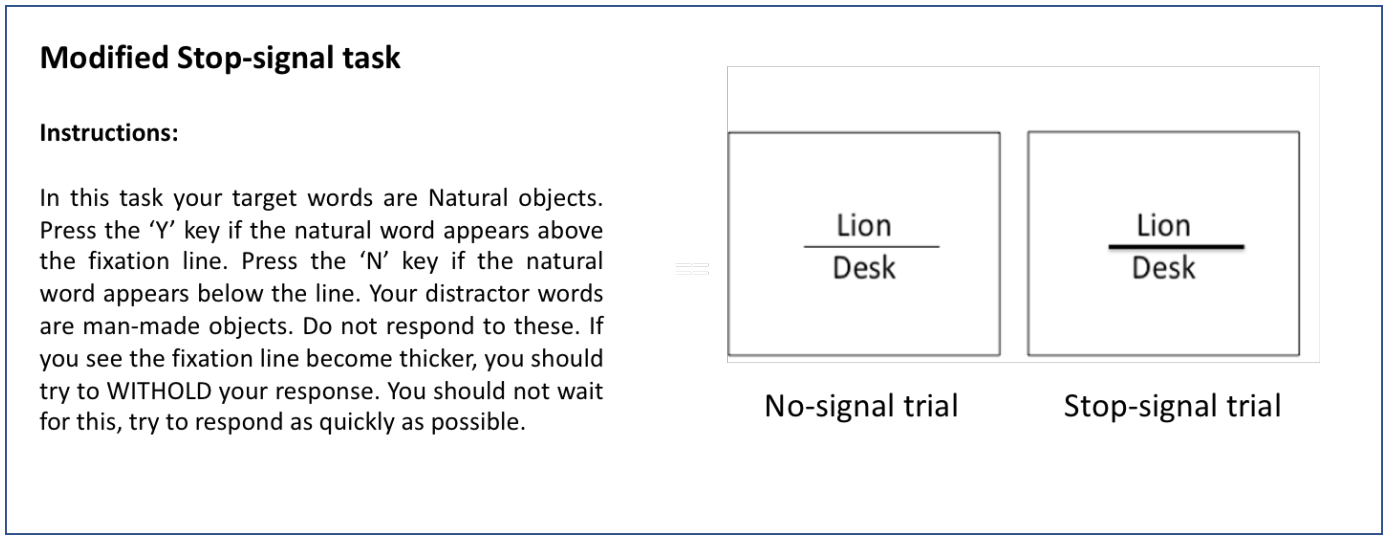


Fig. 2 Task schematic of the SST-anticipation.

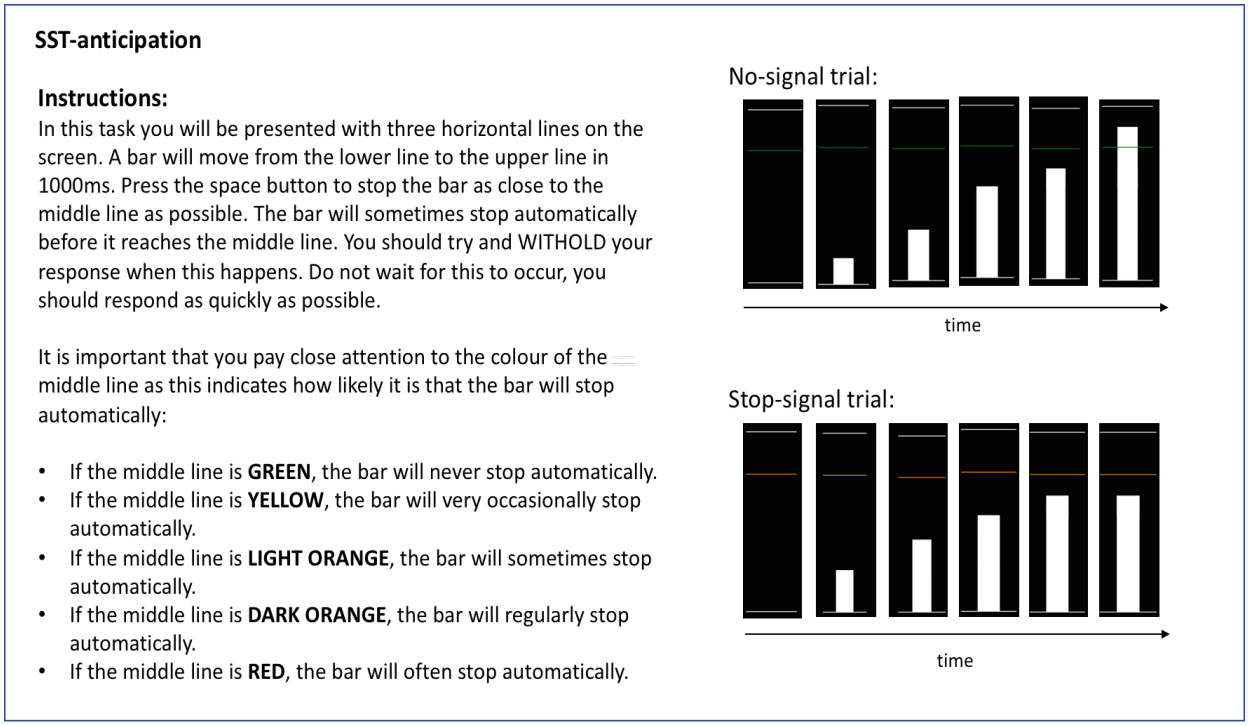


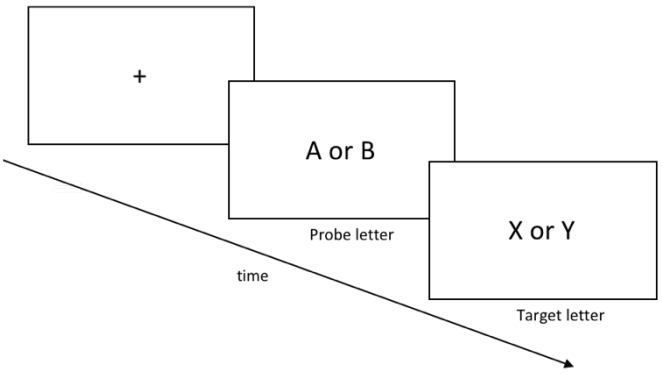
Fig. 3 Task schematic of the AX-CPT

AX-CPT

Instructions:

In this task you are required to respond to letters that appear on the screen. First you will see a fixation cross (+), this is to tell you a trial is about to begin. You will then see a probe letter (A or B), followed by a target letter (X or Y).

If you see the probe letter A then the target letter X you should press the 'V KEY' as fast as you can, when you see the target letter. If you see A followed by Y or B followed by X or Y you should press the 'N KEY' as fast as you can. You should only make responses to the target letters (X or Y).



3.6.2 Results

Sample characteristics

Table 1: Descriptive statistics and Pearson's correlations between age, gender, impulsivity and inhibitory control measures.

	Mean (SD)	2	3	4	5	6	7	8	9
Age	22.13 (7.99)	-.17	-.11	.10	-.03	-.26	.21	-.17	-.15
Gender (M/F)	20/40	-	-.14	-.27*	-.26	-.03	-.02	-.22	.16
Total BIS scores	67.56 (8.58)	-	-	.15	.17	-.16	.20	.12	.07
SSRT (Mod. SST)	391.27 (82.11)	-	-	-	.54**	-.15	.13	-.06	-.14
Proactive slowing (Mod. SST)	226.28 (159.71)	-	-	-	-	-.31*	.28*	-.11	-.10
SSRT (SST-antic.)	243.18 (49.52)	-	-	-	-	-	-.91**	-.04	.11
Proactive slowing (SST-antic.)	46.34 (110.04)	-	-	-	-	-	-	.06	-.17
Reactive control (AX-CPT)	4.22 (3.36)	-	-	-	-	-	-	-	-.01
Proactive slowing (AX-CPT)	-30.62 (84.44)	-	-	-	-	-	-	-	-

*Total BIS scores = Total scores on Barratt Impulsivity scale. Mod. SST = modified Stop-Signal Task. SST-antic. = Stop Signal-anticipation task. AX-CPT = AX-Continuous Performance Task. *p<.05 **p<.01*

Inhibition errors

For the modified-SST, we ran paired samples t-tests to investigate differences in the number of incorrect responses between blocks. Participants made significantly more errors on no-signal trials in the no-signal block (6.69 ±7.96) compared to the stop-signal block (4.37 ±5.76; t (53) = 3.98, p< .001, d = 0.33), which may reflect the slowing of responses in the stop-signal block. In the signal block, participants also made significantly more errors on stop-signal trials (10.91 ±2.32) compared to no-signal trials (4.37 ±5.76; t (53) = -8.13, p<.001, d =1.49).

For the SST-anticipation task, we ran a repeated measures ANOVA to investigate differences in the number of incorrect responses as stop-signal probability increased. There was a significant main effect of stop-signal probability on the number of incorrect responses (F (2, 119) = 122.66, p<.001, η_p^2 = 0.68), which demonstrated that stopping became harder as stop-signal probability increased. Participants made significantly less errors when a 17% stop-signal probability was presented (3.31 ±1.37) compared to 20% (5.88 ±1.66; p<.001), 25% (9.12 ±2.25; p<.001) and 33% stop-signal probability (10.90 ±2.69; p<.001). Participants also made significantly less errors when an 20% stop-signal probability was presented compared to a 25% (p<.001) and 33% stop-signal probability (p<.001). Lastly, participants made significantly less errors when a 25% stop-signal probability was presented compared to 33% (p= .004).

For the AX-CPT, we ran a repeated measures ANOVA to investigate differences in the number of incorrect responses between trial types. There was a significant main effect of trial type on response errors (F (2, 121) = 37.55, p< .001, η_p^2 = 0.39). Participants made significantly more errors on AY trials (4.22 ±3.36) compared to AX trials (2.75 ±3.17; p=.006), BX (0.92 ±1.90; p< .001) and BY trials (0.71 ±1.41; p< .001), which reflects the requirement to over-ride a pre-potent response to respond to the letter 'A.' Participants also made more errors on AX trials compared to BX (p< .001) and BY trials (p<.001). There was no significant difference between BX and BY trials (p=.273).

The reliability of the tasks.

To investigate the internal reliability of reaction times, we calculated Cronbach's alpha using the split-third method. For the modified Stop-Signal task, estimates ranged from .87 to .93 (see table 2). Similarly, for the SST-anticipation task, estimates for internal reliability ranged from .86 to .97 (see table 3). Lastly for the AX-CPT, estimates for internal reliability ranged

from .80 to .88 (see table 4). Therefore, all measures of reaction times were above the .7 cut-off for satisfactory internal reliability (Kline, 1999).

Table 2: Internal reliability of reaction times in modified SST.

	Cronbach's alpha
No-signal block	0.93
Stop-signal block	0.89
Stop-signal block (no-signal trials)	0.87

Table 3: Internal reliability of reaction times split by stop-signal probability (0%, 17%, 20%, 25%, 33%) in the SST-anticipation.

	Cronbach's alpha
0% no-signal trials	0.96
17% no-signal trials	0.86
17% stop and no-signal trials	0.89
20% no-signal trials	0.93
20% stop and no-signal trials	0.92
25% no-signal trials	0.92
25% stop and no-signal trials	0.91
33% no-signal trials	0.97
33% stop and no-signal trials	-[3]

[3] Too few cases to produce Cronbach's alpha due to increased % of stop-signal trials.

Table 4: Internal reliability of reaction times in the AX-CPT.

	Cronbach's alpha
AX RT	0.88
AY RT	0.80
BX RT	0.81
BY RT	0.84

Principal Component Analysis (PCA): reactive and proactive inhibitory measures

Lastly to investigate whether there are independent measures of inhibitory control, we conducted Principal Component Analyses. Based on Kaiser's rule (Kaiser, 1960), we retained components that had eigenvalues of ≥ 1. We also used a scree plot to check the maintenance of components. The Kaiser-Meyer-Olkin measure (KMO) was used to check for sampling adequacy; values of 0.5 to 0.7 are deemed acceptable, values above 0.7 are deemed good to excellent (Hutchenson & Sofroniou, 1999). Bartlett's test of sphericity was also performed to check for adequate correlations between items. We used oblique rotation methods; specifically Oblimin rotation, when performing the PCAs based on the assumption that the factors are correlated. Lastly, since our sample size was 60, factor loadings greater than 0.7 were considered robust factor loadings (see (Stevens, 2009)).

Proactive and Reactive inhibitory control measures in the SST-anticipation, modified SST and AX-CPT.

Firstly, we ran a PCA to investigate if the proactive and reactive measures of inhibitory control loaded onto the same factor across all three tasks. The sampling adequacy was acceptable (KMO =0.53), and Bartlett's test of sphericity demonstrated that correlations between items were large enough for PCA (χ^2 (15) = 90.56, p<.001). The PCA revealed three components which explained 78.37% of the variance; component one Eigenvalue = 2.28 (variance explained 37.95%), component two Eigenvalue = 1.37 (variance explained 22.79%) and component three Eigenvalue = 1.06 (variance explained 17.62%). Table 5 shows the factor loadings, following Oblimin rotation, which suggests that the proactive and reactive control measures load onto the same factor for each task. Therefore, factor one represents proactive and reactive control in the AX-CPT, although proactive slowing is not quite above

the .07 threshold for robust loadings, factor two represents proactive and reactive control in the SST-anticipation and factor three represents these measures in the modified SST.

Table 5: Principal Component Analysis for reactive and proactive measures of inhibition in the SST-anticipation, modified SST and AX-CPT.

	Rotated components		
Variable	Component 1	Component 2	Component 3
Reactive control (AX-CPT)	-.04	-.23	**.80**
Proactive slowing (AX-CPT)	-.12	-.29	-.62
SSRT (SST-antic.)	**-.98**	.03	.02
Proactive slowing (SST-antic.)	**.97**	-.04	.08
SSRT (modified SST)	-.19	**.92**	.10
Proactive slowing (modified SST)	.31	**.76**	-.21

Factors highlighted load above 0.7 and are deemed robust factor loadings.

Proactive and Reactive inhibitory control measures in the SST-anticipation and modified SST.

We also decided to check the independence of these measures using only the Stop-Signal tasks. The sampling adequacy was acceptable (KMO =0.55), and Bartlett's test of sphericity demonstrated that correlations between items were large enough for PCA (χ^2 (6) = 115.84, p<.001). The PCA revealed two components which explained 86.92% of the variance; component one Eigenvalue = 2.21 (variance explained 55.24%), component two Eigenvalue = 1.27 (variance explained 31.68%). Table 6 shows the factor loadings, following Oblimin rotation. However, this suggests that factor one represents proactive and reactive control in the SST-anticipation and factor two represents proactive and reactive control in the modified SST, rather than proactive and reactive control across tasks.

Table 6: Principal Component Analysis for reactive and proactive measures of inhibition in the SST-anticipation and modified SST.

	Rotated components	
Variable	Component 1	Component 2
SSRT (SST-anticipation)	**-.97**	-.02
Proactive slowing (SST-anticipation)	**.98**	-.01
SSRT (modified SST)	-.10	**.92**
Proactive slowing (modified SST)	.13	**.83**

Factors highlighted load above 0.7 and are deemed robust factor loadings.

3.7 Chapter Summary

This chapter contributed to the overall aims of this thesis through the isolation of proactive slowing and reactive control in heavy drinkers. This supports the suggestion that there is an *over-simplification* of inhibitory control in the literature. These findings also strengthened the rationale to examine state fluctuations in these processes in the next chapter, despite the finding of no relationship between individual differences in proactive or reactive control and alcohol use. Furthermore, I was able to take a reliable task forward, which was feasible to adapt in the following manipulation studies.

CHAPTER 4

The effect of alcohol cue-exposure and acute intoxication on inhibitory control processes and *ad libitum* alcohol consumption.

This chapter presents two pre-registered laboratory studies that were published as an original research article in Psychopharmacology (2019, 236(7), 2187-2199). The online supplementary materials are also presented after the article. These studies were pre-registered on Open Science Framework (see Appendices 2 and 3) and data is freely available (links are provided in text). The format of the original article has been modified to match the other chapters in this thesis, however the content remains the same to that of which was published. To summarize contributions to this chapter, I designed both studies which were approved by Andrew Jones, Matt Field and Paul Christiansen. I collected and analyzed the data and wrote the manuscript. Matt Field, Paul Christiansen and Andrew Jones provided feedback on the article before submission to Psychopharmacology and after the peer review process.

Chapter Foreword: This chapter added to the key aim of this thesis by testing transient impairments in inhibitory processes (reactive control, proactive slowing, signal detection) based on seemingly reliable manipulations of alcohol-cues (study one in this chapter) and alcohol intoxication (study two in this chapter). This was based on the successful isolation of proactive slowing and reactive control in chapter 3. The task used to measure these processes in the current chapter was based on the reliability analyses in chapter 3. Lastly, this chapter also contributed to the overall aims of this thesis by investigating whether fluctuations in these inhibitory processes predicted increased alcohol-seeking, and whether these fluctuations mediated the relationship between alcohol-cue exposure/alcohol intoxication and increased alcohol-seeking. Taking into account the null findings in chapter 3, a more objective measure of alcohol-seeking was incorporated into the current studies.

4.1 Abstract

Background: Alcohol intoxication and alcohol cue-exposure impair 'reactive' inhibitory control and increase motivation to drink. However, inhibitory control is a multi-component process that also comprises signal detection and proactive control. It is unknown whether intoxication and cue-exposure selectively influence these sub- processes in heavy drinkers. ***Objectives:*** In two pre-registered studies, we investigated whether exposure to alcohol-related cues (study 1) and alcohol priming (study 2) impair each of these sub-processes of inhibitory control and increase motivation to drink. ***Methods:*** In study 1, 64 heavy drinkers completed a modified Stop-Signal task in an alcohol context (with embedded alcohol-cues) and a neutral context (with embedded neutral-cues) followed by a subjective measure of craving and a bogus taste test to measure *ad-libitum* alcohol consumption. In study 2, 36 heavy drinkers consumed an alcoholic beverage (0.6 g/kg bodyweight), an alcohol-placebo beverage, and water on a within-subjects basis, followed by the modified Stop-Signal task and a bogus taste test. ***Results:*** In study 1, alcohol cue-exposure did not impair inhibitory control sub-processes. Reactive control was unexpectedly better following alcohol cue-exposure (compared to neutral cue-exposure). However, craving and *ad-libitum* consumption increased as expected. In study 2, reactive control was significantly impaired following the alcohol and control primes, relative to the placebo, but there was no effect on proactive slowing or signal detection. As expected, intoxication increased motivation to drink and *ad-libitum* consumption (compared to placebo and control). ***Conclusions/Importance****:* Alcohol intoxication and cue-exposure increase motivation to drink in the absence of impairments in subcomponents of inhibitory control.

4.2 Introduction

Inhibitory control is defined as the (in)ability to suppress, postpone or alter a response that is no longer appropriate (Logan et al., 1984) and can be measured using the Stop-Signal and Go/No-Go computerised tasks. These tasks require the inhibition of a pre-potent motor response following a 'stop-signal' or 'no-go' cue, and provide an index of inhibitory failures (commission errors) or latency to inhibit (Stop Signal Reaction time; SSRT). Theoretical models of addiction suggest a failure or impairment in inhibitory control is a candidate psychological mechanism for the development and maintenance of substance misuse (e.g. (de Wit, 2009; Fillmore, 2003; Goldstein & Volkow, 2002; Yucel et al., 2019). These predictions are supported by empirical evidence indicating that impairments in inhibitory control predict variance in hazardous drinking (Colder & O'Connor, 2002; Houston et al., 2014), and meta-analyses demonstrating that inhibition is impaired in heavy drinkers and substance dependent patients compared to controls (Smith et al., 2014). Longitudinal studies have also demonstrated that impaired inhibitory control predicts the onset of alcohol-related problems in at-risk adolescents (Nigg et al., 2006), the transition from heavy drinking to alcohol dependence (Rubio et al., 2008), and treatment success (Rupp et al., 2016).

Whilst the association between inhibitory control and alcohol (mis)use is seemingly well established, several 'null' findings have also been published (e.g. (Kamarajan et al., 2005; Nederkoorn et al., 2009)), and on closer inspection inhibitory control may only explain a modest amount of variance in substance-use behaviour (Smith et al., 2014). One potential explanation for this is a *simplistic* conceptualization of inhibitory control. Cognitive neuroscience models (Verbruggen, McLaren, et al., 2014) emphasise the importance of the underlying mechanistic processes that contribute to engagement of inhibitory control. For example, SSRT - the estimated time to withhold a response following the presentation of a stop-signal (Brevers et al., 2017) - is regularly used as an index of inhibitory control. However, SSRT represents more than simply the time taken to inhibit a response, because effective stopping relies on initial detection of the stop-signal ('signal detection'), the selection of an appropriate response ('response selection'), followed finally by execution of the stopping response. Importantly, Verbruggen et al (Verbruggen, Stevens, et al., 2014) demonstrated that signal detection contributed to the response inhibition process and can be isolated in Stop-Signal tasks through calculating differences in SSRTs on blocks when the stop-signal is presented in the centre of the screen, compared to blocks when the stop-signal is presented in the periphery. Additionally, although reactive control (SSRT; the act of

stopping) is an important aspect of executive control and has been the focus of most research in substance use, we also have the ability to plan our behaviour and alter this 'proactively' (Verbruggen, McLaren, et al., 2014). This preparatory response has a downstream impact on 'reactive stopping.' Proactive slowing can be inferred by examining the difference in reaction times in blocks where inhibitory signals are present and blocks where these signals are absent and no inhibition is required (Aron, 2011). Indeed, research has shown that participants employ proactive adjustments in order to ready themselves to detect a stop-signal and therefore, slow down their responses (Elchlepp et al., 2016; Verbruggen & Logan, 2009b; Zandbelt et al., 2011). Although these additions may increase task difficulty, we can investigate whether these additional processes influence performance on Stop-Signal tasks and if reactive control alone is limited as a model of executive control (Aron, 2011).

Importantly, both signal detection and proactive control may have a significant role in substance use-behaviour (Brevers et al., 2017). First, substance users selective attention is guided by substance-related cues (Townshend & Duka, 2001) and impaired by alcohol (Plawecki et al., 2018; Roberts et al., 2014), which may make it difficult to detect inhibitory signals in the environment. Second, substance users rarely engage global reactive stopping responses in the real world (i.e. reaching for a glass but then inhibiting), but regularly engage proactive control processes (i.e. preparation in advance, such as declining to order an alcoholic drink). Therefore, to better understand the association between inhibitory control and alcohol use we need to account for the influence of preparation and signal detection on inhibitory control (Verbruggen, McLaren, et al., 2014).

A second issue which may impact the association between inhibitory control and alcohol use is the stability of the processes. The majority of research suggests inhibitory control is stable over long periods. However, more recent evidence suggests inhibitory control may fluctuate over time *within* individuals, suggesting that the capacity to proactively prepare, choose and stop a response are fluid. In a narrative review (Jones, Christiansen, et al., 2013), we identified various situational and internal triggers, for example, alcohol-related cues, alcohol intoxication, ego-depletion and stress, which may cause short term deficits in inhibitory control (see also (de Wit, 2009)). Subsequent empirical research has demonstrated limited evidence for stress-related impairments in inhibitory control (Scholz et al., 2009) and the veracity of the ego-depletion effect is under debate (Hagger et al., 2016). Nevertheless, the effects of acute intoxication and cue-exposure on inhibitory control are seemingly robust; with a systematic review (Weafer & Fillmore, 2016) demonstrating alcohol intoxication

consistently impairs inhibitory control and a recent meta-analyses demonstrating small but robust effects of alcohol-cue exposure on inhibitory control (Jones, Robinson, et al., 2018).

Across the majority of studies included in these evidence syntheses the focus was global reactive control indices (SSRTs or No/Go errors), and currently there is little research investigating the effects of alcohol cues and intoxication on inhibitory sub-processes (specifically, proactive slowing and signal detection). In one study, Sharma (Sharma, 2017) showed how preceding alcohol-cues (compared to neutral cues) impaired the performance of heavy drinkers, but not light drinkers, on a modified Stroop task. These results implied that heavy drinkers were relying on reactive control, whereas light drinkers were employing proactive control to filter out the context of the prior image. Conversely, Campbell et al (Campbell et al., 2017) demonstrated that alcohol intoxication increased motor SSRTs but did not influence proactive slowing. Indeed, this emphasises the simplistic conceptualization of inhibitory control in the majority of prior research and the need to break inhibitory control down into its component processes to further understanding.

Consequently, the current studies aimed to directly investigate the effect of alcohol cue-exposure (study 1), and alcohol intoxication (study 2) on the different components of inhibitory control (namely reactive stopping, signal detection and proactive control), and subsequent craving and *ad-libitum* alcohol consumption. We included these alcohol-seeking measures due to substantial evidence demonstrating that both alcohol-related cues (Fatseas et al., 2015; MacKillop & Lisman, 2007) and alcohol intoxication (Christiansen et al., 2013; de Wit & Chutuape, 1993) increase motivation to consume subsequent alcohol. We also aimed to investigate whether increased alcohol-seeking was the product of impairments in the different components of control as past research has demonstrated that impairments in inhibitory control predict hazardous drinking (Colder & O'Connor, 2002; Houston et al., 2014). We pre-registered the design, statistical power-calculations, hypotheses and analysis strategy, with data freely available on Open Science Framework (study 1: [https://osf.io/qf72a/], study 2: [https://osf.io/dg27x/]).

4.3 Study 1

We hypothesised that exposure to alcohol-related cues compared to neutral cues would (i) impair reactive control, signal detection and proactive slowing; (ii) increase self-reported craving and subsequent *ad-libitum* alcohol consumption. We also hypothesised that (iii) deficits in proactive slowing and signal detection would predict unique variance in alcohol

consumption after controlling for reactive inhibition. Finally, we hypothesised that (iv) the effects of alcohol-cue exposure on *ad libitum* alcohol consumption would be partially mediated by changes in the different components of control.

4.4 Methods

4.4.1 Participants

Heavy drinkers (N=64; 37 females, 27 males) took part in a laboratory study across two sessions, approximately one week apart. Participants were aged between 18 and 59 (M = 23.73, SD = 9.33) and were recruited from the University of Liverpool and wider community through online advertisements. We conducted a power analysis to detect a within-subjects interaction (d = .39, α = .05, 1-β = 90%) based on a pooled effect size from studies which have examined the effect of alcohol-related cues on inhibitory control in heavy drinkers (e.g. (Czapla et al., 2015; Kreusch, Vilenne, & Quartemont, 2013)). Heavy drinking was defined using UK government guidelines: males and females who consume > 14 UK units of alcohol per week (1 UK unit = 8g of pure alcohol). Eligibility criteria included; age 18 or over, a fluent English speaker and a self-reported motivation to reduce their alcohol consumption. We recruited individuals who reported motivation to restrict consumption as these individuals should be employing inhibitory control to restrict their intake (Hofmann, Schmeichel, & Baddeley, 2012). Exclusion criteria included; self-reported current or previous diagnosis of Substance Use Disorder, ADHD, psychiatric disorder, a current/recent illness (e.g. flu) that could increase sensitivity to alcohol, taking medications (e.g. antidepressants) that are adversely affected by alcohol, pregnancy or breastfeeding. The study was approved by the University of Liverpool's local ethics committee.

4.4.2 Materials

Questionnaires

Participants completed a battery of questionnaires; this included a two-week *Timeline follow back* (TLFB: (Sobell & Sobell, 1990)) to measure retrospective alcohol consumption in units, the *Alcohol Use Disorders Identification Test* (AUDIT: (Saunders et al., 1993)) to measure hazardous drinking (study 1: α = .66, study 2: α = .66), the *Brief Comprehensive Effects of Alcohol Questionnaire* (B-CEAQ: (Ham et al., 2005)) to measure alcohol outcome expectancies (study 1: α = .84 study 2: α = .80), the *Temptation Restraint Inventory* (TRI: (Collins & Lapp, 1992)) to measure drinking restraint (preoccupation with and efforts to

reduce drinking) (study 1: α's > .61, study 2: α's > .54) and the *Barratt Impulsivity Scale* (BIS: (Patton et al., 1995)) to measure self-reported impulsivity across three dimensions (Motor, Non-planning and Attentional) (study 1: α's > .61, study 2: α's > .44).

To measure self-reported craving before and after the Stop-Signal task, participants completed the *Approach and Avoidance of Alcohol Questionnaire* 'right now' version (AAAQ: (McEvoy et al., 2004)) which consists of three sub-scales of craving (Inclined/Indulgent, Obsessed/Compelled, Resolved/Regulated) (study 1: α's > .64, study 2: α's > .78). Participants also completed a funnelled debrief to measure awareness of the experimental aims of the study. This included an open question asking what the purpose of the experiment was and two fixed-response questions asking the purpose of the computer task and the taste test (see supplementary materials).

Modified Stop-Signal task (SST;(Verbruggen, Stevens, et al., 2014)).

Participants completed a modified Stop-Signal task, designed to isolate proactive slowing, reactive control and signal detection. At the beginning of each trial, a white fixation line appeared in the middle of the screen for 500ms, as well as a white border around the edge of the screen display. Following these, two words appeared, one immediately above the line and one immediately below the fixation line. These words described natural- (e.g. lion, swan) or man-made (e.g. desk, shed) objects, based on (Verbruggen, Stevens, et al., 2014). Natural words were assigned as targets and participants had to respond as quickly as possible to their position in relation to the line (above or below) by a key press. Man-made words were distractors. Depending on condition, a neutral-related image (e.g. a scene from an office) or alcohol-related image (e.g. a scene from a bar) appeared in the background on each trial. There were 10 of each image type, and they were 230 mm x 130 mm in size. The task consisted of three blocks (no-signal block, central-signal block, peripheral-signal block), which were presented in a randomised, counterbalanced order.

No-signal block: In this block participants had to identify the position of the target word in relation to the line without interruption on 100% of trials (128 in total).

Central-signal block: In this block participants had to identify the position of the target word in relation to the line without interruption on 75% of trials (96 in total). The remaining 25% (32 in total) trials were stop-signal trials, in which the white fixation line between the words increased in size by 300%. Participants were told to try and withhold their response to the target word position if this happened.

Peripheral-signal block: In this block participants identified the position of the target word in relation to the line without interruption on 75% of trials (96 in total). The remaining 25% (32 in total) trials were stop signal trials, in which the white square around the edge of the display increased in size by 300%. Participants were told to try and withhold their response to the target word position if this happened.

Participants were also given standard stop-signal instructions in which they were explicitly told that they should not to wait for the signal and should instead, respond as quickly as possible. In both the central-signal and peripheral signal block the delay between presentation of the target and distractor word and the increase in size of the stop signals (fixation line or square around the display) was adjusted on a trial-by-trial basis using a tracking procedure (Verbruggen & Logan, 2009a). In each block the initial delay was 250ms, if participants failed to inhibit the delay decreased by 50ms making subsequent inhibition easier, if participants successfully inhibited then the delay increased by 50ms making subsequent inhibition more difficult.

In line with our pre-registration, reactive control was inferred as the mean SSRT (Verbruggen et al., 2013) collapsed across central and peripheral signal blocks. However, we also examined SSRTs based only on central signal blocks in order to provide a more direct comparison with previous literature. Proactive slowing was inferred from the degree of reaction time slowing on both stop-signal blocks compared to no-signal blocks (RTstop-signal – RTno-signal). Signal detection was inferred from the difference in SSRT (SSRTperiphery signal – SSRTcentral signal) between central-signal and periphery-signal blocks. The effects of alcohol-cues on each process were measured by comparing performance across conditions (alcohol context, neutral context).

Ad libitum taste test

Participants received 250 ml of chilled Skol beer (2.8% vol. ABV) and 250 ml of chilled fresh orange juice (non-alcoholic beverage). They were not informed of the brands used and were given each drink simultaneously in unmarked glasses. Participants were asked to taste and rate the drinks on various gustatory dimensions e.g. '*How bitter did you find the drink?*' using visual analogue scales and were told to '*drink as much or as little as you like in order to make accurate judgements*'. Before completion, participants were also told that alcohol would impair performance on the next task, in which they had the opportunity to win small amounts of money, in order to increase their motivation to restrict their intake (taken from

(Christiansen et al., 2013; Field & Jones, 2017)). The volume of each drink consumed was recorded unobtrusively at the end of each session, and *ad-libitum* alcohol consumption was expressed as the amount of beer as a percentage of total fluid consumed.

4.4.3 Procedure

Participants attended two sessions approximately one week apart, the order of which was counterbalanced. One session was completed in a standard neutral laboratory, the other was completed in the University of Liverpool's Bar Laboratory (https://www.liverpool.ac.uk/psychology-health-and-society/departments/psychological-sciences/facilities/bar-lab/) which resembles a typical UK bar containing advertisements for alcohol, beer pumps etc. Participants were breathalysed at the beginning of each session and were required to have a breath alcohol concentration (BAC) of 0.0mg/l in order to take part. Participants first provided demographic information and completed the battery of questionnaires measuring alcohol use and personality and the AAAQ to measure craving before the SST. Before each block of the task, participants were asked to smell a drink and allow a small amount to touch their lips (beer in the alcohol session, water in the neutral session), to increase cue-reactivity further (see (Field & Jones, 2017)). Following the SST, participants completed a second AAAQ to measure craving following the task. They then completed the taste test followed by a Balloon Analogue Risk task (BART; (Lejuez, Aklin, Zvolensky, & Pedulla, 2003)). During this task, participants had to click a mouse to pump up 10 simulated balloons. Each pump was worth £0.05 which they could collect in a "permanent bank." However, if the balloon burst before collection, participants lost the money from that trial. This task was presented to ensure participants believed our cover story, that alcohol might impair their performance. Our hypotheses did not concern performance on this task, and as a result it is not reported here (see supplementary materials for further details). Participants then provided a final breath alcohol sample, and in the final session completed a funnelled debrief assessing awareness of experimental measures (see supplementary analyses).

4.4.4 Data reduction and analysis

For the Stop-Signal task, outliers were removed following criteria suggested in previous research (Field & Jones, 2017; Verbruggen & De Houwer, 2007). Reaction times that were greater than 2000ms or less than 100ms were removed; as were reaction times that were

greater than 2.5 standard deviations greater or less than individual means. We also checked for outliers during examination of box-and-whisker plots.[4] Two participants were removed from the Stop-Signal task analysis as the data did not record for one block. One participant did not complete the taste test during the neutral session as they stated they had not eaten during the day of testing. Details of how each hypothesis was analysed is included in the pre-registration. Post-hoc comparisons were carried out using LSD tests.

4.5 Results

4.5.1 Sample characteristics (see supplementary table 1)

Participants consumed 53.64 (±35.64) units on average in the two weeks prior to their participation in the study, and reported an average AUDIT score of 12.59 (± 4.65), indicative of hazardous drinking. An independent t-test revealed no significant differences in AUDIT scores between males (13.48 ±5.21) and females (11.95 ±4.16; t (62) = 1.31, p = .195, d = 0.33). However, males consumed significantly more units (68.87 ±46.16) in the two weeks prior to the study compared to females (42.53 ±19.56; t (33) = 2.79, p = .009, d = 0.71).

4.5.2 Hypothesis 1: Does alcohol cue-exposure cause deficits in inhibitory processes (see table 1)

Deficits in signal detection and reactive control were analysed using a 2 (block: central signal, peripheral signal) x 2 (condition: alcohol cue-exposure, neutral cue-exposure) repeated measures ANOVA on SSRTs. This revealed a significant main effect of block, (F (1, 61) = 36.99, p< .001, η_p^2= .38) where SSRTs were significantly faster for central compared to peripheral blocks. This indicates greater reactive stopping when the stop-signal was presented centrally compared to in the periphery. There was also a main effect of condition, (F (1, 61) = 4.52, p= .038, η_p^2= .07) but contradictory to our hypothesis, SSRTs were significantly faster (indicating better reactive stopping) during alcohol-cue exposure compared to neutral cue-exposure. Furthermore, there was no interaction between block and condition (F (1, 61) = 3.02, p= .087, η_p^2= .05) suggesting that cue-exposure did not impair signal detection. We also compared SSRTs in central stop-signal blocks only and this revealed no significant differences in SSRTs following alcohol cue-exposure compared to

[4] Two participants were identified during the outlier analysis with a high frequency of errors. However, their removal did not change the pattern of results.

neutral cue-exposure (t (61) = -.74, p= .463, d= -0.11) again suggesting that alcohol-cues did not impair reactive control.

Proactive slowing was analysed using a 2 (block: no-signal block, central and peripheral signal blocks) x 2 (condition: alcohol cue-exposure, neutral cue-exposure) repeated measures ANOVA on reaction times. This showed a main effect of block, (F (1, 61) = 134.47, p< .001, η_p^2= .69) whereby participants slowed down their responses more in the stop-signal blocks compared to the no-signal blocks indicative of proactive slowing. Furthermore, there was a main effect of condition, (F (1, 61) = 5.34, p= .024, η_p^2= .08) whereby participants were slower to respond during neutral cue-exposure compared to alcohol cue-exposure. However, there was no significant interaction between block and condition, (F (1, 61) = 1.11, p= .295, η_p^2= .02) suggesting that alcohol cue-exposure did not impair proactive slowing.

Table 1: Descriptive statistics for SSRTs and mean go-reaction times (ms) shown separately for each condition (values are Mean, SD)

	Alcohol cue-exposure	Neutral cue-exposure
SSRT (central)	426.13 (108.39)	437.32 (102.34)
SSRT (peripheral)	475.48 (132.71)	526.12 (156.64)
Overall SSRT	450.81 (103.27)	481.72 (116.30)
No-signal block RT	714.75 (101.78)	757.15 (114.72)
Signal block RT (central)	946.11 (233.52)	963.67 (182.66)
Signal block RT (periphery)	945.29 (229.26)	971.08 (168.05)

Lower score = faster SSRT. Overall SSRT = mean of the periphery and central SSRTs

4.5.3 Hypothesis 2: Does alcohol cue-exposure increase craving and ad-libitum alcohol consumption (see table 2)

To examine whether alcohol cue-exposure increased craving, scores on the AAAQ were analysed using a 3 (subscale: mean scores on inclined/indulgent, obsessed/compelled, resolved/regulated) x 2 (time: pre-manipulation, post-manipulation) x 2 (condition: alcohol

cue-exposure, neutral cue-exposure) repeated measures ANOVA. This revealed that there was no main effect of condition (F (1, 63) = 1.31, p= .257, η_p^2= .02) or time (F (1, 63) = 2.41, p= .125, η_p^2 = .04). However, there were significant condition x time (F (1, 63) = 11.96, p= .001, η_p^2 = .16) and condition x time x AAAQ subscale (F (2, 114) = 5.95, p= .005, η_p^2 = .09) interactions.

To examine these interactions further, a 2 x 2 ANOVA was conducted on each subscale separately. For the *Inclined/Indulgent* subscale there was no main effect of condition (F (1, 63) = 0.79, p= .378, η_p^2 = .01). However, there was a main effect of time (F (1, 63) = 4.15, p= .046, η_p^2 = .06) with scores decreasing post-manipulation. There was also a significant condition x time interaction (F (1, 63) = 13.45, p= .001, η_p^2 = .18). This revealed a decrease from pre- to post-manipulation following neutral cue-exposure (p<.001) but no difference between pre- and post-manipulation following alcohol-cue exposure (p=.279). This suggests craving did not significantly increase following alcohol-cue exposure. Lastly, there was no difference at post-manipulation between the two conditions (p=.437). For the *Obsessed/Compelled* subscale, there was a condition x time interaction (F (1, 63) = 6.82, p= .011, η_p^2 = .10) demonstrating that participants reported greater craving post-manipulation compared to pre-manipulation following alcohol cue-exposure (p= .025) but no difference following neutral cue-exposure (p= .768). There was also no difference between the conditions at post-manipulation (p = .524). Lastly, there was only a main effect of time on the *Resolved/Regulated* scale (F (1, 63) = 6.21, p= .015, η_p^2 = .09) which showed scores decreased at post-manipulation in both conditions.

To examine differences in *ad-libitum* alcohol consumption we conducted paired samples t-tests on beer consumed (as a percentage of total fluid). This revealed that participants drank significantly more beer following alcohol cue-exposure compared to neutral cue-exposure (*t* (62) = 2.66, p= .01, *d* = 0.34; see figure 1). Finally, there was no significant difference in ratings of alcohol pleasantness following alcohol cue-exposure (6.33 ± 2.31) compared to neutral cue-exposure (6.11 ± 2.13; *t* (62) = 0.96, p=.34, *d*= 0.12) (see supplementary materials for further details).

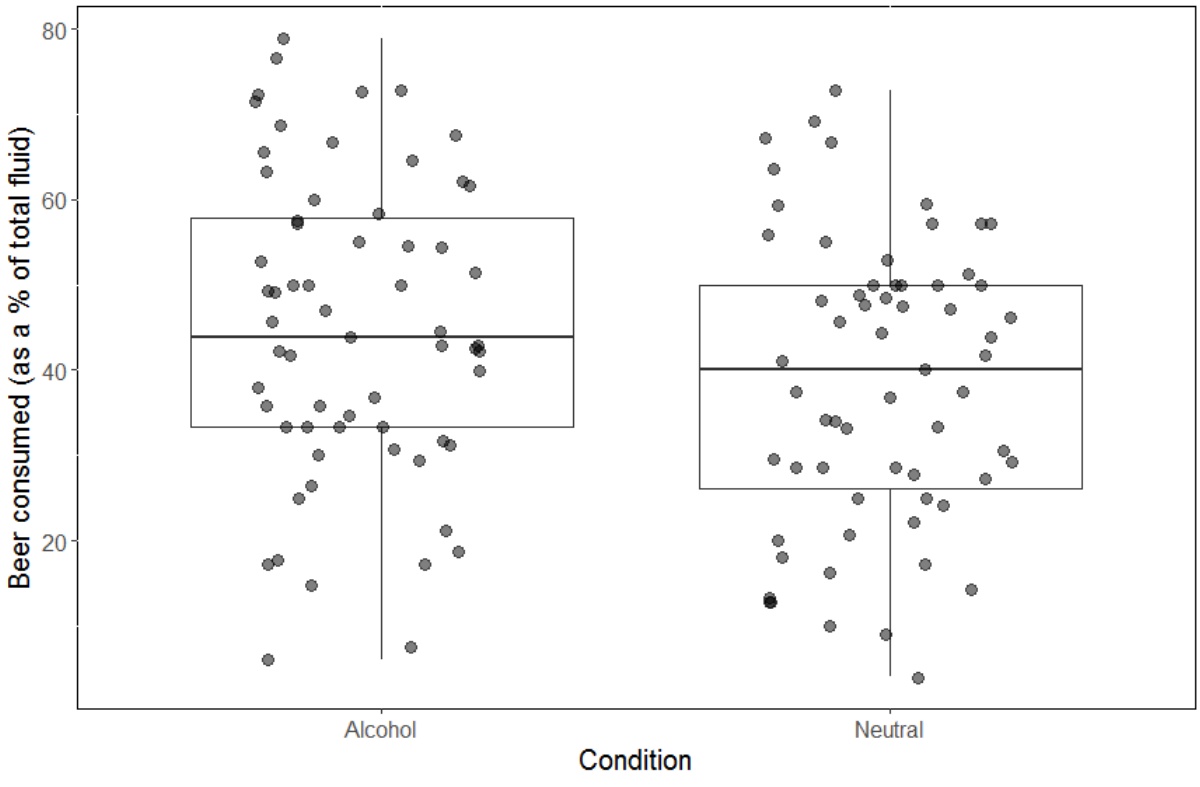
We also hypothesised that deficits in proactive slowing and signal detection would predict unique variance in alcohol consumption after controlling for reactive inhibition, and that the effects of alcohol cues on *ad libitum* alcohol consumption would be partially mediated by changes in the different components of control. However, we did not demonstrate impairments due to alcohol cue-exposure and deficits in inhibitory control did

not predict alcohol consumption. Hence, we do not meet the assumptions required to examine within-subjects mediation (see supplementary materials).

Table 2: AAAQ scores before and after the modified Stop-Signal Task split by experimental condition (values are mean, SD).

	Alcohol cue-exposure		Neutral cue-exposure	
	Pre-task	Post-task	Pre-task	Post-task
Inclined/Indulgent	4.61 (1.54)	4.74 (1.58)	5.05 (1.44)	4.59 (1.68)
Obsessed/Compelled	0.75 (0.89)	0.95 (1.05)	0.91 (1.04)	0.88 (1.03)
Resolved/Regulated	1.28 (1.14)	1.15 (1.22)	1.38 (1.22)	1.38 (1.22)

Fig 1 Boxplot to show beer consumed as a percentage of total fluid following alcohol cue-exposure and neutral cue-exposure (N=63)



4.6 Interim discussion

Study one demonstrates that alcohol cue-exposure did not impair inhibitory sub-processes. Indeed, reactive control was unexpectedly better following alcohol cue-exposure (compared to neutral cue-exposure) when examining central and peripheral stop-signal blocks, although there was no difference when analysing central blocks only. Furthermore, although there was the presence of proactive slowing and increased signal detection of central stop-signals (compared to periphery), neither proactive slowing nor signal detection were directly impaired by alcohol-cues. In line with previous research, alcohol cue-exposure increased craving (albeit weakly) and subsequent *ad-libitum* alcohol consumption. However, this was not the result of impairments in inhibitory sub-processes.

4.7 Study 2

In study two, we administered a control, placebo-alcohol and alcohol prime to investigate the pharmacological and anticipated effects of alcohol on inhibitory sub-processes and motivation to drink. Typical alcohol priming studies compare the effects of an alcohol dose and a placebo dose to investigate the pharmacological effects of alcohol (e.g. (Fillmore et al., 2009; Marczinski et al., 2005; Weafer & Fillmore, 2008)). However, this comparison has low ecological validity as in the real world it is likely that the effect of alcohol is the result of both the pharmacological and the anticipated effects. Therefore, with the addition of a control condition we are able to distinguish the anticipated from the pharmacological effects of alcohol (Christiansen et al., 2013).

We hypothesised that acute alcohol intoxication compared to placebo and control would (i) cause deficits in reactive control, signal detection and proactive slowing; (ii) increase alcohol-seeking measures[5]. We also hypothesised that (iii) following alcohol intoxication, proactive slowing, signal detection and reactive control would predict unique variance in alcohol consumption. Finally, we hypothesised that (iv) the effects of alcohol intoxication on *ad libitum* alcohol consumption would be partially mediated by changes in the different components of control.

[5] We also predicted that the placebo-alcohol beverage would increase subjective intoxication ratings, motivation to drink, beer consumed in the taste test and deficits in proactive and reactive control compared to the control condition, but not to the same extent as alcohol.

4.8 Methods

4.8.1 Participants

Heavy drinkers (N = 36; 19 males) took part in a laboratory study with three sessions, approximately one week apart. Participants were aged between 18 and 44 (M = 24.75, SD = ±7.33). The number of participants was decided upon using a power calculation to find a medium effect size (d = .50) at α = .05, and 90% power. Studies have demonstrated larger effect sizes of alcohol impairments on inhibitory control (Stroop) tasks (e.g. (Rose & Duka, 2008) d = .89)), however as no research has examined the effects on inhibitory subcomponents we opted for a more conservative estimate of d = .50. Inclusion exclusion criteria, and recruitment strategy were the same as study 1.

4.8.2 Materials

Questionnaires

Participants completed the same questionnaires and awareness of experimental aims questions (see supplementary materials) that are described in the method of study 1. They also completed the *Subjective intoxication scales (SIS; (Duka et al., 1998))* to measure subjective feelings of 'lightheaded,' 'irritable', 'stimulated', 'alert', 'relaxed' and 'contented' following alcohol priming. We also asked participants how many alcohol units they believed they had consumed in the priming drink in each session.

Stop-signal task (SST; (Verbruggen, Stevens, et al., 2014))

Participants completed a modified Stop-Signal task, which was near identical to task 1. The only difference being that we removed the alcohol and neutral-related images in order to prevent contamination of findings with cue-exposure. Therefore, the task was presented on a black background across each block and session.

4.8.3 Procedure

Participants attended three sessions (alcohol, placebo and control) in a neutral laboratory. Each session took place between 12pm and 6pm and had to be at least one week apart. The sessions were completed in a pseudo-counterbalanced order. In line with previous studies participants completed the control session first, followed by either the placebo or alcohol session in a counterbalanced order. Participants were informed that the experiment was investigating the effect of a high, low and no dose of alcohol on taste perception. Participants

were breathalysed at the beginning of each session and BAC of 0.0mg/l was required in order to take part.

Participants first completed the demographic questions and a battery of questionnaires measuring personality and alcohol use (first session only). They then completed the AAAQ and dependent on condition, received either the alcohol, placebo or control drink (in 2 glasses) and were asked to consume this within 10 minutes, followed by a 20-minute absorption period.

The alcoholic drink contained vodka (Smirnoff Red, 37.5% alcohol by volume (ABV)) and chilled tonic water. The alcohol dose was calculated as 0.6g/kg of body weight (maximum dose of 200 ml vodka / 8 UK units) and the drink mixed one-part vodka, three parts tonic water. The placebo-alcohol drink contained chilled tonic water, the total volume of which was the same as the alcoholic drink. Vodka mist was sprayed onto the surface of the drink and smeared onto the rim of the glass to simulate the smell and taste of alcohol. Tabasco sauce was also added to the drink to give the burning sensation of alcohol. The control drink consisted of chilled water; the total volume was identical to the alcoholic and placebo drink. This procedure is similar to previous research carried out (e.g. (Christiansen et al., 2013)).

Participants then completed the AAAQ, SIS, and provided a breath alcohol sample, before completing the SST. Following the SST, participants completed the *ad-libitum* taste test (see study 1 method) and were informed that alcohol may impair their performance on the last task, in which they had the opportunity to win small amounts of money. Lastly, participants completed the BART task (see study 1 procedure/supplementary materials) and provided a final breath alcohol sample.

4.8.4 Data Analysis

SST data was handled using the same procedures as study 1. Two participants were excluded from the SST analysis due to outliers. One participant was removed from the analysis of the taste test as they did not complete this during one session. Further details on the analysis of each hypothesis can be found in the pre-registration.

4.9 Results

4.9.1 Sample characteristics (see supplementary table 1)

Participants consumed an average of 48.90 (±25.72) UK units in the two weeks prior to the

first session of the study and reported a mean AUDIT score of 11.78 (±4.81), indicative of hazardous drinking. There was no significant difference in AUDIT scores between males (11.32 ±3.89) and females (12.29 ±5.75; *t* (34) = -.60, p= .55, *d*= 0.20), however males did consume significantly more units (60.32 ±25.68) than females (36.15, ±19.43; *t* (34) = 3.16, p = .003, *d*= 1.06) in the two weeks prior to taking part. There were no significant differences in drinking patterns of the participants across the two studies (see supplementary materials).

4.9.2 Hypothesis 1: Does alcohol intoxication cause deficits in inhibitory processes (see table 3)

Deficits in signal detection and reactive control were analysed using a 2 (block: central, periphery) x 3 (condition: control, alcohol, placebo) repeated measures ANOVA on SSRTs. There was a significant main effect of block (F (1, 33) = 48.05, p< .001, η_p^2= .59) with SSRTs significantly faster in the central stop-signal blocks compared to the peripheral stop-signal blocks. Similar to study 1, this indicates that reactive stopping was better when stop-signals were presented centrally compared to in the periphery. There was also a main effect of condition (F (2, 66) = 3.44, p= .038, η_p^2= .09) which revealed that as predicted SSRTs were significantly slower (indicating poorer reactive control) following alcohol intoxication compared to the placebo (p= .008). However, there was no difference following alcohol compared to the control prime (p= .841). Contrary to predictions, SSRTs were also significantly faster following the placebo compared to the control (p= .033) suggesting that the anticipated effects of alcohol did not impair reactive control. Lastly, there was no interaction between block and condition (F (2, 66) = 2.09, p = .132, η_p^2= .06) indicating alcohol intoxication did not impair signal detection. For direct comparisons with previous research we also investigated differences in SSRTs computed from central stop-signal blocks *only*. This also revealed a main effect of condition (F (2, 66) = 3.39, p= .04, η_p^2= .09) which demonstrated that SSRTs were significantly slower following alcohol compared to a placebo (p=.018) but only demonstrated weak evidence for a difference following alcohol compared to a control (p= .084). However, there was also no difference between control compared to the placebo primes (p= .449), again demonstrating no anticipated impairing effects of alcohol on reactive control.

Deficits in proactive slowing were analysed using a 2 (block: no-signal, stop-signal) x 3 (condition: control, alcohol, placebo) repeated measures ANOVA on mean go-reaction times. In line with study 1, this revealed a significant main effect of block (F (1, 33) = 81.13,

p<.001, η_p^2= .71). Participants responded significantly faster in the no-signal block compared to the stop-signal blocks indicating the presence of proactive slowing. There was also a main effect of condition (F (2, 66) = 3.64, p=.032, η_p^2= .10) which revealed that participants were slower to respond in the control session compared to the alcohol (p=.011). However, there was no difference following the alcohol prime compared to the placebo (p=.292) or following the placebo compared to the control (p=.132). Most importantly, there was no interaction between block and condition (F (2, 66) = 0.89, p= .415, η_p^2= .03) suggesting that alcohol intoxication did not impair proactive slowing.

Table 3: Descriptive statistics for SSRTs and mean go-reaction times (ms) shown separately for each condition (values are Mean, SD)

	Control	Alcohol	Placebo
SSRT (central)	378.39 (76.26)	410.39 (81.39)	364.86 (84.59)
SSRT (periphery)	512.11 (176.87)	490.48 (174.51)	431.50 (105.64)
Overall SSRT	445.25 (109.54)	450.44 (109.69)	398.18 (85.58)
No-signal block RT	708.67 (90.77)	670.85 (77.59)	691.27 (113.87)
Signal block RT(central)	948.71 (180.38)	887.37 (187.88)	879.85 (192.15)
Signal block RT(periphery)	976.68 (170.86)	894.70 (218.66)	940.19 (206.74)

Lower score = faster SSRT. Overall SSRT = mean of the periphery and central SSRTs

4.9.3 Hypothesis 2: Does alcohol intoxication increase alcohol-seeking and consumption (see Table 4)

Changes in craving subscales were assessed using a 3 (subscales: mean score on inclined/indulgent, obsessed/compelled and resolved/regulated) x 3 (condition: control, alcohol, placebo) x 2 (time: pre-drink, post-drink) repeated measures ANOVA. There was no main effect of condition, (F (2, 70) = 0.90, p= .41, η_p^2= .03) or time, (F (1, 35) = 2.54, p= .12, η_p^2= .07). However, there was a significant condition x time interaction (F (2, 70) = 7.96, p=.001, η_p^2= .19).

To examine the interaction, we conducted 3 (condition: control, alcohol, placebo) x 2 (time: pre-drink, post-drink) repeated measures ANOVAs on each subscale individually. For

both the *Inclined/Indulgent* and *Obsessed/Compelled* subscales, there was a significant condition x time interaction (Inclined (F (2, 70) = 5.71, p= .005, η_p^2= .14); Obsessed (F (2, 70) = 3.98, p=.023, η_p^2=.10)). The nature of these interactions demonstrated that participants reported lower scores on the Inclined subscale at post-control compared to pre-control (p=.005) but there were no significant differences across time in the alcohol or placebo sessions (ps >.05). Across conditions, participants reported higher scores on the *Inclined/Indulgent* subscale following the alcohol prime compared to the placebo (p=.044) but there were no other significant differences between conditions. On the *Obsessed/Compelled* subscale, participants reported higher scores at post-drink in the alcohol session compared to pre-alcohol (p=.018) but there was no difference following the placebo or control drinks. Participants also reported higher scores following alcohol compared to the control (p= .004) but there were no other significant differences across conditions. For the *Resolved/Regulated* subscale, there was only a main effect of time (F (1, 35) = 10.90, p= .002, η_p^2= .24) which demonstrated that participants felt less avoidant towards alcohol post-drinks compared to pre-drink. Notably, there were no significant differences in any of these measures pre-drink (ps >.05).

Table 4: Descriptive Statistics for craving scores before and after the priming drinks (Values Are Mean, SD)

	Inclined/Indulgent	Obsessed/Compelled	Resolved/Regulated
Pre-control	5.12 (1.92)	1.22 (1.65)	1.33 (1.37)
Post-control	4.34 (2.36)	1.11 (1.59)	1.18 (1.33)
Pre-placebo	4.74 (1.89)	1.38 (1.87)	1.48 (1.45)
Post-placebo	4.27 (2.23)	1.41 (1.88)	1.08 (1.28)
Pre-alcohol	4.68 (1.67)	1.41 (1.80)	1.34 (1.47)
Post-alcohol	4.98 (2.11)	1.83 (2.04)	1.13 (1.50)

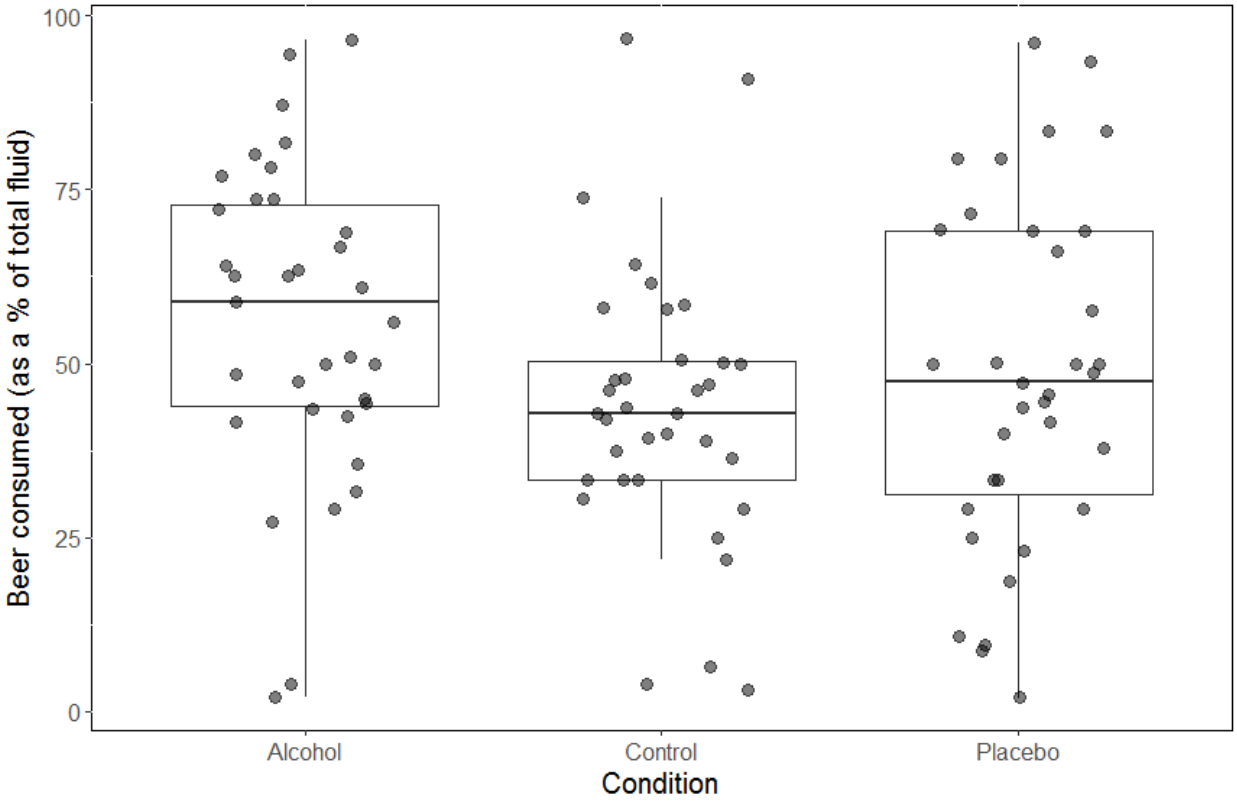
We also investigated if alcohol priming increased *ad-libitum* alcohol consumption. There was a main effect of condition on beer consumed in the taste test (F (2, 68) = 5.98, p=.004, η_p^2=.15). Participants drank significantly more beer following the alcohol prime

compared to both control (p=.002) and placebo (p=.045) primes, however, there was no difference following the control compared to placebo prime (p=.199) (see figure 2). There was no main effect of condition on pleasantness ratings of beer (F (2, 68) = 1.89, p=.159, η_p^2=.05).

For BACs a 3 (Condition: alcohol, placebo, control) x 2 (time: post-drink, end of session) repeated measures ANOVA with 3 levels demonstrated a significant main effect of condition, (F (1, 34) = 399.94, p< .001, η_p^2= .92) with significantly higher BACs following the alcohol prime compared to the placebo (p< .001) and control (p< .001) primes. As expected there was no significant difference following the placebo prime compared to the control (p= .518). There was also a significant main effect of time (F (1, 34) = 27.94, p < .001, η_p^2= .45). As expected, BACs were significantly higher at end of session compared to post-drink. Finally, there was also a significant condition x time interaction (F (2, 68) = 3.95, p = .038, η_p^2= .10) with significantly higher BACs following the alcohol prime (0.27 ±0.09) compared to the placebo-alcohol (0.00 ±0.00) and control (0.00 ±0.00) at post-drink (p<.001). Following the taste test, BACs were also significantly higher at the end of the session following the alcohol prime (0.32 ±0.09) compared to the placebo (0.02 ±0.03; p<.001) and control (0.02 ±0.04; p<.001). There was no difference between the placebo and control drinks at post drink or end of session (p=.518). Analyses for subjective intoxication and estimation of units can be found in the supplementary materials.

We also hypothesised that deficits in inhibitory sub-processes would predict unique variance in beer consumed during the bogus taste test and that the effect of alcohol intoxication on beer consumed would be partially mediated by the different components of control. However, the effect of alcohol priming on SSRTs was weak and deficits in inhibitory sub-processes did not predict unique variance in beer consumption, therefore these analyses are included in supplementary materials.

Fig 2 Boxplot of the mean consumption of beer (as a % of total fluid consumed) in the ad libitum taste test during the control, alcohol and placebo sessions (N=35)[6]



4.10 Discussion

The current studies aimed to investigate the effect of alcohol cue-exposure and alcohol intoxication on proactive slowing, reactive control, signal detection and subsequent craving and *ad-libitum* alcohol consumption. In study 1, there were no impairments of proactive slowing or signal detection following alcohol cue-exposure (compared to neutral cue-exposure), and contrary to hypotheses reactive control was unexpectedly faster following exposure to alcohol-cues compared to neutral-cues. Alcohol-cues did have a weak effect on craving (on the Obsessive scale of the AAAQ) and increased *ad-libitum* alcohol consumption. In study 2, neither proactive slowing or signal detection were impaired by alcohol intoxication. SSRTs were slower (indicative of worse inhibitory control) following alcohol compared to the placebo prime supporting our hypothesis, but there was no difference

[6] The removal of outliers from the control session did not significantly influence the comparison in beer consumption following the alcohol prime compared to the control, however the comparison following the alcohol prime compared to the placebo was no longer significant.

compared to the control condition. SSRTs were also significantly faster following the placebo compared to the control suggesting the anticipated effects of alcohol did not impair reactive control. As expected, alcohol priming did increase self-reported craving and *ad-libitum* alcohol consumption (compared to placebo and control).

Taken together, these findings provide limited support for theoretical models which suggest that inhibitory control is a state variable which fluctuates in response to internal (alcohol intoxication) and environmental (cue-exposure) events (de Wit, 2009; Jones, Christiansen, et al., 2013). Specifically, we failed to replicate numerous studies which have demonstrated impairments following alcohol cue-exposure in both non-dependent (Field & Jones, 2017; Kreusch, Vilenne, & Quartemont, 2013; Monk, Sunley, Qureshi, & Heim, 2016; Petit et al., 2012; Weafer & Fillmore, 2012) and dependent drinkers (Gauggel et al., 2010; Muraven & Shmueli, 2006). Indeed, SSRTs were faster during alcohol cue-exposure compared to neutral cue-exposure when analysing both central and peripheral stop-signal blocks and there was no difference across central blocks only. However, a recent meta-analysis (Jones, Robinson, et al., 2018) demonstrated this effect is likely to be small in magnitude (Standardised Mean Difference = 0.21[7]), and other research has also failed to demonstrate these effects across non-dependent and dependent drinkers (Jones, Rose, et al., 2013; Nederkoorn et al., 2009).

Importantly, we demonstrated support that acute alcohol intoxication impaired reactive control compared to a placebo which supports previous research (e.g. (Fillmore et al., 2009; Marczinski et al., 2005; Weafer & Fillmore, 2008)). However, the addition of a control group revealed that the effect of alcohol intoxication on SSRTs is limited. We also failed to support the observation that placebo intoxication impairs inhibitory control compared to control groups (Christiansen et al., 2016) as when analysing both central and periphery blocks, SSRTs were unexpectedly faster following the placebo compared to the control, although there was no difference across central blocks only. These results may be partially explained by compensatory effects in which participants in the placebo condition may attempt to compensate for impairments (Fillmore, Mulvihill, & Vogel-Sprott, 1994), and research demonstrates that individuals who show larger compensatory effects following a placebo usually show more tolerance to impairment following alcohol (Testa et al., 2006). Furthermore, although Campbell et al (Campbell et al., 2017) reported an impairment of motor (but not saccadic) inhibition following alcohol intoxication, their effect was smaller

[7] Note that this meta-analysis was published after recruitment of this study, hence the larger estimate of d=.39 used for the power calculation.

than predicted. This led them to suggest that there is a lack of power and the existence of publication bias in the literature. Similarly, Jones et al (Jones, Robinson, et al., 2018) also recently questioned the clinical significance of any impairments due to the small effect size and lack of associations with substance use behaviours.

Our findings provide support for recent cognitive models which suggest that inhibitory control is a multi-process behaviour (Verbruggen, McLaren, et al., 2014). We were able to adapt tasks from the literature to isolate signal detection and proactive control, and across both studies showed that heavy drinkers demonstrate proactive slowing when inhibition is more likely and also increased stopping times when stop-signals are in the periphery, which demonstrates the contribution of signal detection to reactive stopping processes. Notably, the requirement of participants to detect a visual central or peripheral stop-signal and differentiate between natural and man-made words may have improved the ecological validity of the task as in the real world, signal detection and response inhibition occur under complex conditions (e.g. multiple environmental demands) and in 'noisy' surroundings (Verbruggen, Stevens, et al., 2014). However, this may have contributed to a failure to replicate previous findings due to the increased task difficulty and therefore, attention requirements. The use of a visual stop-signal did however decrease the need for divided attention as this was the same modality as the go-stimuli (Verbruggen, Stevens, et al., 2014). Furthermore, it should be noted that Campbell et al (Campbell et al., 2017) also failed to demonstrate a reliable decrease in proactive slowing following alcohol priming, however as previously noted there is a lack of research focusing on this aspect of executive control and therefore it is still possible that proactive slowing is impaired by alcohol. Despite limited evidence for impairments *within* individuals, future research should therefore investigate whether these impairments are exacerbated in clinical populations, or evident in individuals who do not drink to hazardous levels (Sharma, 2017).

Finally, our findings provide further empirical support of studies which have demonstrated that alcohol-related cues (Fatseas et al., 2015; Koordeman, Anschutz, & Engels, 2011; MacKillop & Lisman, 2007) and alcohol intoxication (e.g. (Christiansen et al., 2013; de Wit & Chutuape, 1993; Rose & Grunsell, 2008)) increase subsequent alcohol seeking. Furthermore, although the placebo-alcohol increased subjective feelings of light-headedness supporting previous research (e.g. (Rose et al., 2013)), there was no difference in beer consumption following the placebo-alcohol and control as predicted. Nevertheless, this replicates the findings of Christiansen et al (Christiansen et al., 2013) and implies that the pharmacological effects (not the anticipated effects) of alcohol are key to the priming effect

on subsequent motivation to consume alcohol. However, those studies (e.g. (Marlatt, Demming, & Reid, 1973)) which have found an increase in alcohol consumption following a placebo compared to a control tend to have a short interval between administration of the drinks and the taste test. In both Christiansen et al's study (Christiansen et al., 2013) and the current study, there was a longer interval (approximately 40 minutes passed between beverage consumption, the Stop-Signal task and the bogus taste test in the current study), therefore, the effect of the placebo on subsequent motivation to drink may have reduced over time (Christiansen et al., 2013). Additionally, despite the increase in *ad-libitum* consumption in both studies we did not demonstrate robust increases in craving. Although contradictory to our hypothesis and previous findings (e.g. (Christiansen et al., 2013; Fatseas et al., 2015; Field & Jones, 2017; Rose et al., 2013)), this suggests that alcohol seeking can increase without an accompanied increase in self-reported craving, which has also been reported in previous studies (e.g. (Wiers, Rinck, Kordts, Houben, & Strack, 2010) see also (Tiffany, 1990; Wiers et al., 2007)).

Our findings should be interpreted in light of limitations. In study 1 our cue-exposure manipulation may not have been strong enough to influence inhibitory control. Although we used similar methods to (Field & Jones, 2017), their manipulation may have been strengthened by asking participants to sniff beer after every 16 trials rather than at the beginning of each block, and responding directly to alcohol related cues (rather than neutral words). Additionally, their sample had greater levels of weekly alcohol consumption (~34.18 units) and AUDIT scores (~14.18), suggesting these individuals demonstrate a greater sensitivity to cue-reactivity (Herrmann, Weijers, Wiesbeck, Böning, & Fallgatter, 2001). Second, we are unable to separate the effects of these different cue modalities on inhibitory processes and *ad-libitum* alcohol consumption and future studies should attempt to isolate these effects (Monk et al., 2016).

In conclusion, alcohol-related cues and alcohol priming increase motivation to consume subsequent alcohol, however this is unlikely due to an impairment in the ability to inhibit behaviour(s). Future research should attempt to clarify the mechanisms underlying this relationship and investigate additional processes which may lead to impairments in inhibitory control, in order to increase our understanding of hazardous drinking.

4.11 Supplementary Information

4.11.1 Methods

Balloon Analogue Risk Task (BART; ((Lejuez et al., 2003))

In both studies, participants completed a short cognitive task in which they had to click a mouse to pump up simulated balloons. They were presented with one balloon per trial and completed 10 trials. Each time participants clicked to pump up the balloon, the balloon increased in size and they hypothetically collected $0.05 in a temporary bank. They could transfer this money to a "permanent" bank by clicking collect. However, they were informed that if the balloon bursts, they would lose the money stored in the temporary bank. Once the balloon had burst or the participant had collected the money, a new trial began whereby the size of the balloon was reset and the temporary bank was set back to $0. We programmed the balloons to burst on a variable ratio, with 64 pumps as the average explosion point. Participants completed this task after the bogus taste test in both studies; they were told that alcohol would impair their performance on this task in which they had the opportunity to win small amounts of money in order to increase their motivation to reduce their intake (see (Christiansen et al., 2013; Field & Jones, 2017)). Actual performance on this task was of secondary importance but data is available upon request.

4.11.2 Results

Sample characteristics (see table 1)

We conducted independent samples t-tests to compare the participants in study 1 (alcohol-cue exposure) to participants in study 2 (alcohol priming) on baseline variables and drinking variables. There were no significant differences in the age of participants (t (98) = -.56, p= .575, d= .12), AUDIT scores (t (98) = .83, p= .408, d= .17), units consumed in the two weeks prior to the study (t (98) = .70, p= .485, d= .15) or total scores on the Barratt Impulsivity Scale (t (98) = .27, p= .788, d= .06).

Table 1: Sample characteristics and baseline variables of participant samples in study 1 and study 2 split by gender (values are mean, SD)

	Study 1			Study 2		
	Males	Females	Sample	Males	Females	Sample
N	27	37	64	19	17	36
Age	22.04(9.26)	24.97(9.30)	23.73(9.33)	26.11(8.05)	23.24(6.33)	24.75(7.33)
AUDIT	13.48(5.21)	11.95(4.16)	12.59(4.65)	11.32(3.89)	12.29(5.75)	11.78(4.81)
TLFB	68.87(46.16)	42.53(19.56)	53.64(35.64)	60.32(25.68)	36.15(19.43)	48.90(25.72)
BIS	69.81(10.54)	65.22(8.40)	67.16(9.56)	66.00(11.68)	69.65(9.97)	67.72(10.91)

Audit=Alcohol Use Disorder Identification Test. Scores above 8 are indicative of hazardous drinking. TLFB=Timeline follow back. Units consumed in 14 days prior to taking part. BIS=Total scores on Barratt Impulsivity Scale.

4.11.3 Study 1

Hypothesis 2: Does alcohol-cue exposure increase craving and ad-libitum alcohol consumption?

Participants also had marginally significantly higher BACs following alcohol cue-exposure (0.03 ± 0.04) compared to neutral cue-exposure (0.02 ± 0.03; t (62) = 2.00, p=.05, d= 0.33).

Hypothesis 3: Do deficits in proactive slowing and signal detection predict unique variance in alcohol consumption after controlling for reactive inhibition?

We conducted multiple regression analyses on each condition separately. Variation Inflation Factors (VIFs) ranged between 1.05 and 1.43 suggesting there were no issues with multi-collinearity. The full regression model did not predict a significant amount of variance (R^2 = .05) in beer consumed (as a percentage of total fluid consumed) following alcohol-cue exposure (F (3, 57) = 0.90, p= .447). SSRT (β= .22, p= .154, 95% CI -.02 to .09), signal detection (β= -.07, p= .593, 95% CI -.05 to .03) or proactive slowing (β= -.01, p= .958, 95% CI -.03 to .03) were not significant predictors. Similarly, the overall regression model did not predict a significant level of variance (R^2 =.12) in beer consumed following neutral cue-exposure (F (3, 57) = 2.29, p= .088). Again, neither SSRT (β= -.18, p= .219, 95% CI -.07 to

.02), signal detection (β= -.19, p= .196, 95% CI -.06 to .01) or proactive slowing (β= -.09, p= .498, 95% CI -.04 to .02) were significant predictors.

Hypothesis 5: The effects of alcohol cues on ad libitum alcohol consumption will be partially mediated by changes in the different components of control (see figure 1-3).

To examine whether changes in the different components of control partially mediate the effect of alcohol-cue exposure on *ad libitum* alcohol consumption, we ran a within-subjects mediation analysis using MEMORE macro for SPSS (Montoya & Hayes, 2016). We used bias-corrected, bootstrapped (1000 samples) confidence intervals. Firstly, there was no indirect effect of alcohol-cue exposure on beer consumed during the bogus taste test via SSRT (B= -1.02 (SE= 1.00), 95% CI -3.47 to 0.63). However, the direct effect of alcohol-cue exposure on beer consumed was significant after controlling for SSRT (B= 7.80 (SE= 2.50), 95% CI 2.80 to 12.79). Secondly, there was also no indirect effect of alcohol-cue exposure on *ad libitum* consumption via proactive slowing (B= 0.46 (SE= 0.69), 95% CI -0.30 to 2.79), although there was a direct effect after controlling for proactive slowing (B=6.32 (SE= 2.48), 95% CI 1.36 to 11.28). Thirdly, there was no indirect effect via signal detection (B= 0.31 (SE= 0.79), 95% CI -0.76 to 2.78), however the direct effect was significant after controlling for signal detection (B= 6.46 (SE= 2.50), 95% CI 1.45 to 11.47). Lastly, there was a significant total effect of alcohol cue-exposure on *ad libitum* beer consumption (B= 6.77 (SE= 2.46), 95% CI 1.86 to 11.69).

Fig 1: The direct and indirect effect of alcohol-cue exposure on *ad libitum* alcohol consumption via SSRT.

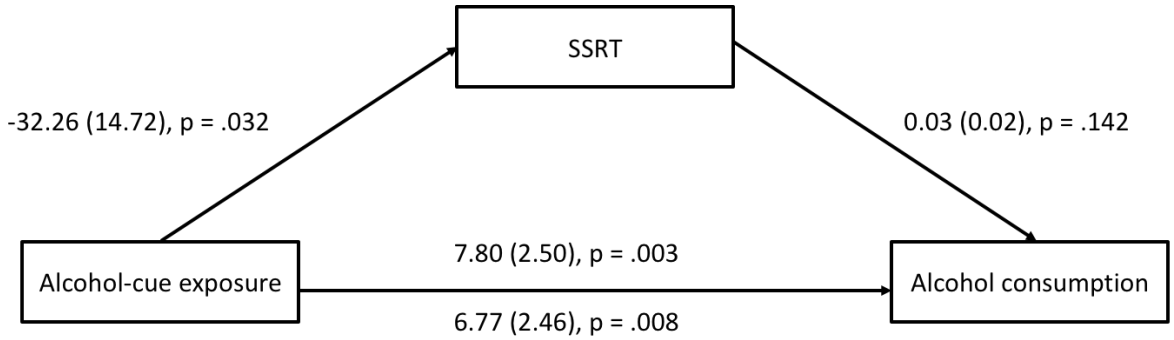


Fig 2: The direct and indirect effect of alcohol-cue exposure on *ad libitum* alcohol consumption via proactive slowing.

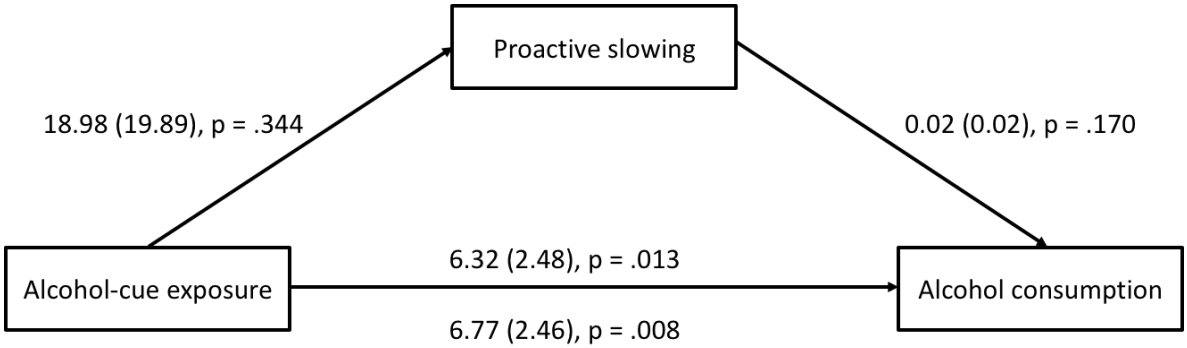
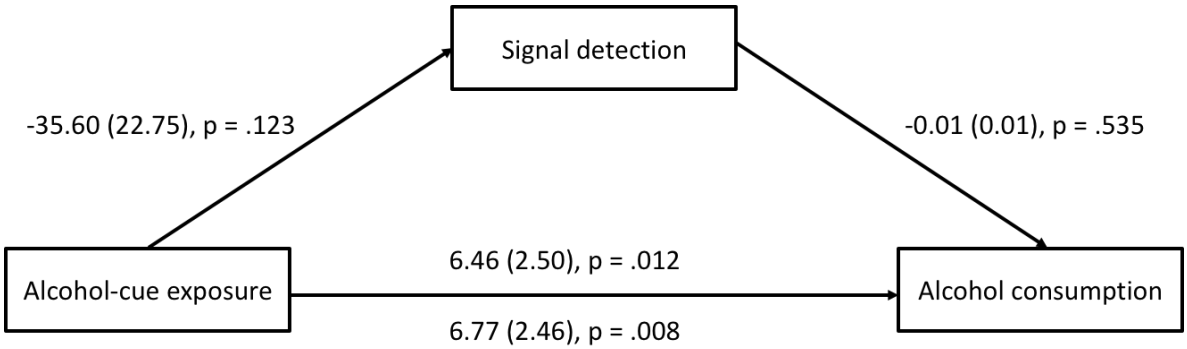


Fig 3: The direct and indirect effect of alcohol-cue exposure on *ad libitum* alcohol consumption via signal detection.



4.11.4 Study 2

Hypothesis 2: Does alcohol intoxication increase alcohol-seeking measures?

There was a significant main effect of condition of subjective feelings of light-headedness ($F(2, 70) = 39.23$, $p < .001$, $\eta_p^2 = .53$). Participants felt significantly more light headed following the alcohol priming drink (38.97 ±27.82) compared to the control (2.40 ±5.49; $p < .001$) and placebo-alcohol drink (12.89 ±19.69; $p < .001$). Participants also reported feeling significantly more light headed following the placebo-alcohol drink compared to the control ($p = .004$). There was also a significant main effect of condition of subjective feelings of alertness, ($F(2, 60) = 10.61$, $p < .001$, $\eta_p^2 = .23$). Participants reported feeling significantly more alert following the control drink (65.71, ±26.10) compared to the alcohol (42.44 ±26.17; $p < .001$) and placebo-alcohol drinks (54.56 ±23.10; $p = .023$). Participants also reported feeling significantly more alert following the placebo-alcohol drink compared to the

alcohol drink (p = .008). There were no other significant differences in the subjective intoxication measures between sessions (ps >.05).

There was a significant main effect of condition on estimation of units in the priming drink (F (2, 60) = 92.84, p < .001, η_p^2= .73). Participants thought they had consumed significantly more units in the alcohol drink (4.61 ±2.38) compared to the placebo-alcohol (2.69 ±1.63; p < .001) and control drink (0.00 ±0.00; p < .001). They also reported consuming significantly more units in the placebo-alcohol drink compared to the control drink (p < .001). Notably, two participants believed that the placebo drink contained no alcohol but removal of these did not significantly influence our results.

Hypothesis 4: Do inhibitory sub processes predict variance in beer consumed during bogus taste test?

We ran multiple regression analyses on each condition separately. VIFs ranged between 1.04 to 2.58 suggesting no issues with multi-collinearity. The full regression model did not predict a significant amount of variance in beer consumed (as a percentage of total fluid consumed) in the alcohol session (R^2 = 0.06, F (3, 29) = 0.64, p= .598). SSRT (β= -.33, p= .195, 95% CI -.15 to .03), signal detection (β= .25, p= .323, 95% CI -.03 to .09) and proactive slowing (β= .10, p= .608, 95% CI -.03 to .05) were not significant predictors of beer consumed following alcohol intoxication. The full regression model also did not predict a significant amount of variance in beer consumed during the placebo session (R^2 = .08, F (3, 29) = 0.89, p= .457). Neither SSRT (β = .20, p = .339, 95% CI -06 to .17), signal detection (β =-.26, p = .186, 95% CI -.19 to .04) nor proactive slowing (β = .03, p= .90, 95% CI -.05 to .06) were significant predictors of beer consumed following the placebo-alcohol prime. Lastly, the full regression model also did not predict significant variance in beer consumed during the control session (R^2 = .01, F (3, 29) = 0.06, p= .982). Again, neither SSRT (β = .06, p= .839, 95% CI -.10 to .12), signal detection (β = -.10, p= .729, 95% CI -.08 to .06) nor proactive slowing (β = .02, p =.922, 95% CI -.05 to .05) were significant predictors of beer consumed following the control prime.

Hypothesis 5: The effect of alcohol intoxication on beer consumed would be partially mediated by the different components of control.

Alcohol-control priming (see figure 4-6)

There was no indirect effect of alcohol priming (compared to the control) on *ad libitum* consumption via SSRT (B = -.20 (SE = 0.99), 95% CI -5.58 to 0.79). However, the direct effect of alcohol priming on consumption was significant after controlling for SSRT (B = 13.02 (SE = 4.04), 95% CI 4.76 to 21.28). Similarly, there was no indirect effect of alcohol priming on consumption via proactive slowing (B = 0.77 (SE = 1.15), 95% CI -0.67 to 4.06), although the direct effect was significant after controlling for proactive slowing (B= 12.05 (SE = 4.05), 95% CI 3.77 to 20.32). Thirdly, there was no indirect effect via signal detection (B = 0.15 (SE= 1.14), 95% CI -1.73 to 3.07), however, the direct effect was significant after controlling for signal detection (B= 12.67 (SE = 4.10), 95% CI 4.30 to 21.03). Lastly, there was a significant total effect (B = 12.82 (SE = 3.94), 95% CI 4.80 to 20.84) of alcohol priming on *ad libitum* alcohol consumption.

Fig 4: The direct and indirect effect of alcohol priming (control-alcohol) on *ad libitum* alcohol consumption via SSRT.

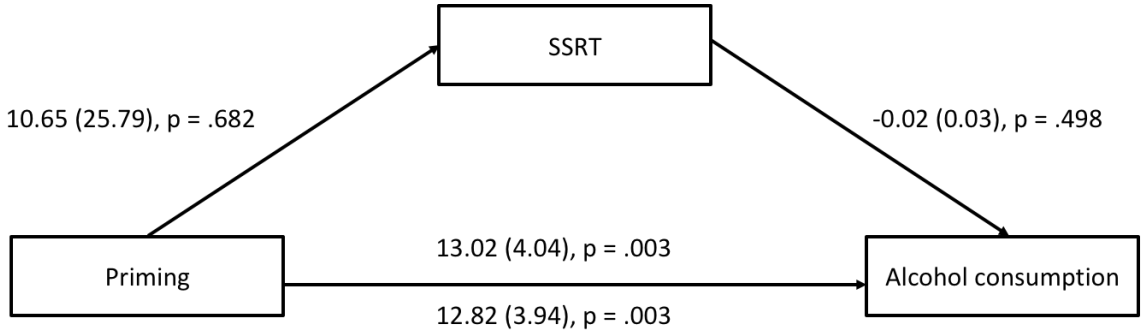


Fig 5: The direct and indirect effect of alcohol priming (control-alcohol) on *ad libitum* alcohol consumption via Proactive slowing.

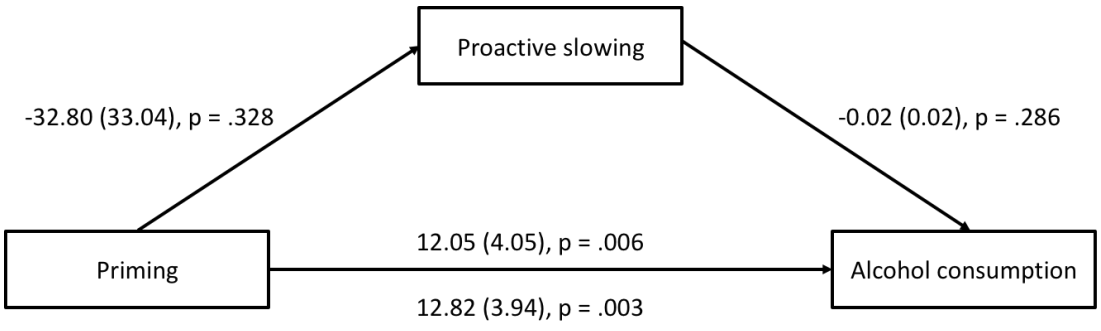
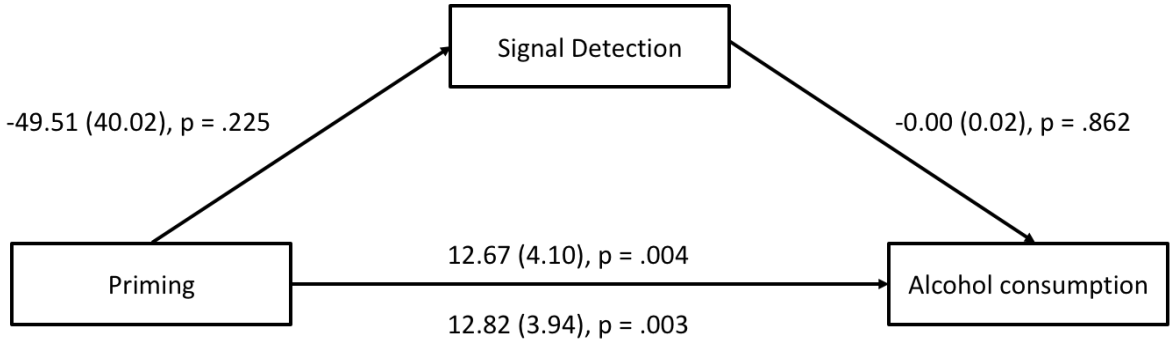


Fig 6: The direct and indirect effect of alcohol priming (control-alcohol) on *ad libitum* alcohol consumption via Signal detection.



Alcohol-placebo priming (see figure 7-9)

Furthermore, there was no indirect effect of priming (alcohol compared to placebo) on beer consumed via SSRT (B = 1.27 (SE = 2.96), 95% CI -2.04 to 11.09) or direct effect of priming on beer consumed after controlling for SSRT (B= 6.84 (SE= 4.72), 95% CI -2.80 to 16.47). There was also no indirect effect of priming on beer consumed via proactive slowing (B = -0.04 (SE = 0.82), 95% CI -2.24 to 1.06) or no direct effect after controlling for proactive slowing (B = 8.14 (SE = 4.21), 95% CI -0.46 to 16.74). Additionally, there was no indirect effect of priming on beer consumed via signal detection (B= 0.01 (SE = 0.87), 95% CI -1.85 to 1.89) and no direct effect after controlling for signal detection (B= 8.09 (SE = 4.23), 95% CI -0.55 to 16.74). Lastly, there was no total effect of priming on beer consumed (B = 8.10 (SE = 4.09), 95% CI -0.23 to 16.44).

Fig 7: The direct and indirect effect of priming (alcohol-placebo) on *ad libitum* alcohol consumption via SSRT.

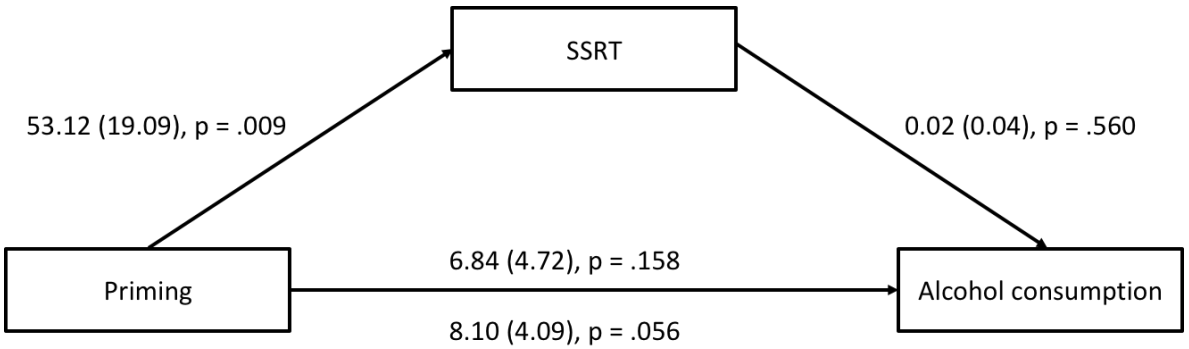


Fig 8: The direct and indirect effect of priming (alcohol-placebo) on *ad libitum* alcohol consumption via proactive slowing.

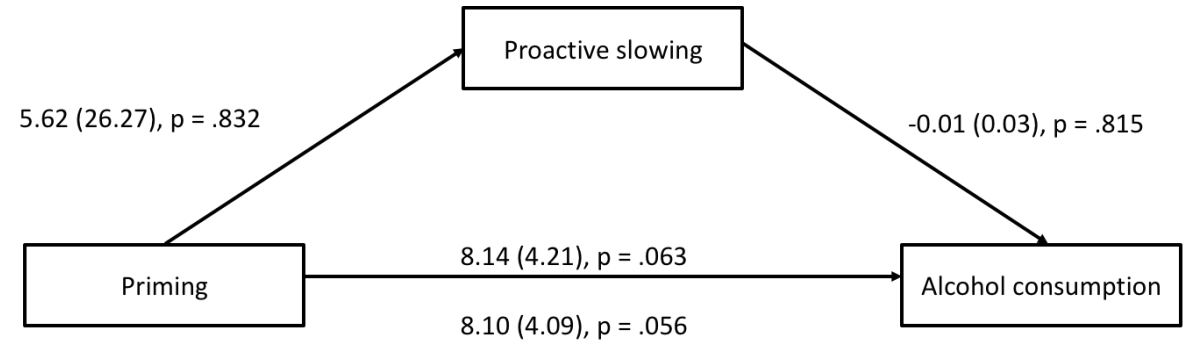
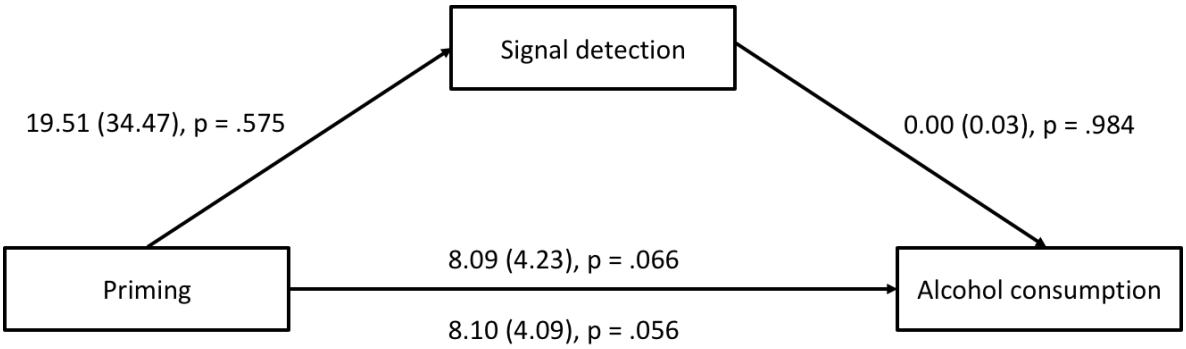


Fig 9: The direct and indirect effect of priming (alcohol-placebo) on *ad libitum* alcohol consumption via signal detection.



Placebo-control priming (see figure 10-12).

Lastly, there was no indirect effect of priming (placebo compared to control) on consumption via SSRT (B= -0.44 (SE= 1.58), 95% CI -3.96 to 2.60) or no direct effect of priming on consumption after controlling for SSRT (B = 5.16 (SE = 4.00), 95% CI -3.01 to 13.33). There was also no indirect effect via proactive slowing (B = 0.12 (SE = 1.00), 95% CI -1.60 to 2.17) or direct effect after controlling for proactive slowing (B = 4.60 (SE = 3.87), 95% CI -3.31 to 12.50). Thirdly, there was no indirect effect via signal detection (B = 2.23 (SE = 2.26), 95% CI -0.90 to 8.00) or direct effect after controlling for signal detection (B = 2.49 (SE = 4.09), 95% CI -5.86 to 10.83). Lastly, there was no significant total effect of priming on alcohol consumption (B = 4.72 (SE = 3.67), 95% CI -2.76 to 12.19).

Fig 10: The direct and indirect effect of priming (placebo-control) on *ad libitum* alcohol consumption via SSRT.

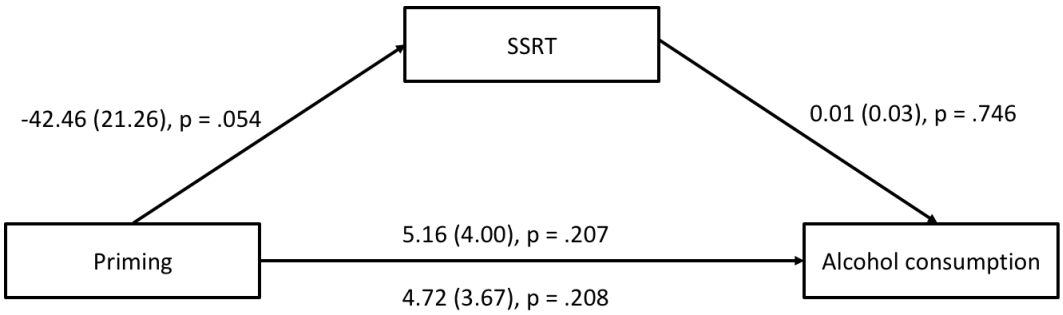


Fig 11: The direct and indirect effect of priming (placebo-control) on *ad libitum* alcohol consumption via proactive slowing.

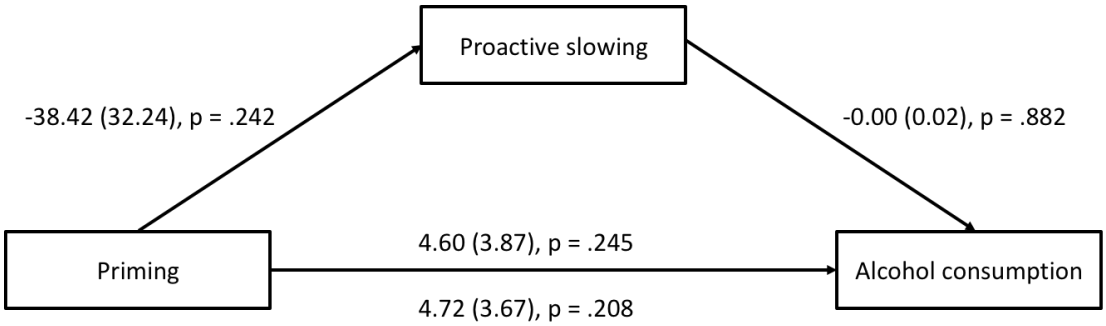
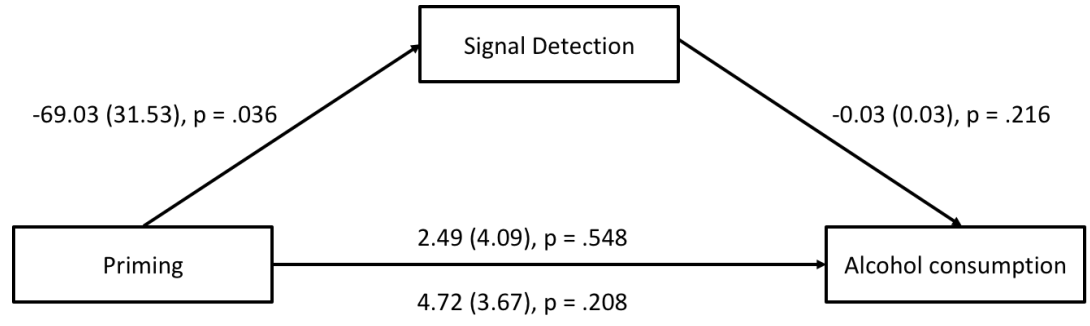


Fig 12: The direct and indirect effect of priming (placebo-control) on *ad libitum* alcohol consumption via signal detection.



4.11.5 Awareness of experimental aims

In both studies we checked participants' awareness of our experimental aims and none of the participants guessed the full aims (inferred from an open ended question). However, in study 1, 13 participants guessed the aim of the taste test was to measure how much they drank, but removing these had no significant effect on the results. Additionally, we removed 17

participants who correctly selected that the purpose of the computer task was to '*Assess my behavioural impulsivity (response inhibition).'* This removed the main effect of condition on SSRTs, however contrary to predictions this had shown SSRTs were faster following alcohol-cue exposure (compared to neutral-cue exposure). Similarly, in study 2, five participants guessed the aim of the taste test but when removed, the main effect of condition remained significant. Eight participants also correctly guessed the purpose of the computer task but removal of these only altered the main effect of condition on proactive slowing which had simply shown participants were slower to respond overall in the control priming session compared to the alcohol priming session.

4.11.6 exploratory analyses

We also conducted exploratory analyses to investigate the effect of alcohol-cue exposure (study 1) and alcohol intoxication (study 2) on the number of errors made during the Stop-Signal task. This also allowed an investigation into differences in the number of errors between stop-signal blocks.

Study 1

To investigate the effect of alcohol-cue exposure on the number of errors made during the stop-signal task, we conducted a 2 (block: Central, Peripheral) x 2 (condition: Alcohol-cue exposure, Neutral-cue exposure) repeated measures ANOVA on incorrect no-signal trials and incorrect stop-signal trials. This showed no significant main effect of block on the number of incorrect no-signal responses ($F (1, 61) = 0.15$, $p= .703$, $\eta_p^2= .002$). There was however, a main effect of condition ($F (1, 61) = 8.09$, $p= .006$, $\eta_p^2= .12$) which revealed that participants made significantly less errors to no-signal trials in the bar laboratory compared to the neutral laboratory. Finally, there was no significant interaction between block and condition ($F (1, 61) = 0.11$, $p= .746$, $\eta_p^2= .002$). With regards to incorrect responses on stop-signal trials, there was a significant main effect of block ($F (1, 61) = 10.72$, $p= .002$, $\eta_p^2= .15$), which revealed that participants made more errors in the central blocks compared to the peripheral blocks. However, there was no main effect of condition ($F (1, 61) = 0.84$, $p= .362$, $\eta_p^2= .01$) or interaction ($F (1, 61) = 2.21$, $p= .142$, $\eta_p^2= .04$). Lastly, a paired samples t-test revealed no significant differences in the number of incorrect responses in the no-signal block in the bar laboratory compared to the neutral laboratory ($t (61) = -1.49$, $p= .141$, $d= .17$).

Table 2: The number of incorrect responses shown separately for each block of the SST and experimental condition (values are mean, SD).

	Alcohol cue-exposure	Neutral cue-exposure
No-signal block	7.35 (4.97)	8.21 (4.83)
No-signal trials (central block)	6.06 (6.92)	7.74 (4.62)
Stop-signal trials (central block)	11.81 (4.40)	11.82 (3.66)
No-signal trials (periphery block)	5.68 (4.47)	7.69 (4.70)
Stop-signal trials (periphery block)	12.58 (4.53)	13.56 (5.24)

Study 2

We ran a 2 (block; Central, Peripheral) x 3 (condition: alcohol, placebo, control) repeated measures ANOVA on incorrect no-signal trials and incorrect stop-signal trials. This revealed there was no main effect of block on incorrect no-signal trials ($F (1, 33) = 1.27$, $p= .269$, $\eta_p^2=.04$), nor was there an effect of condition ($F (2, 66) = 1.29$, $p= .284$, $\eta_p^2= .04$) or an interaction ($F (2, 66) = 0.01$, $p= .989$, $\eta_p^2= .00$). With regards to incorrect stop-signal trials, there was a main effect of block ($F (1, 33) = 9.39$, $p= .004$, $\eta_p^2= .22$) which showed that participants made less errors in central blocks compared to periphery blocks. There was also a main effect of condition ($F (2, 66) = 4.95$, $p= .01$, $\eta_p^2= .13$) which demonstrated that participants made more errors on stop-signal trials following alcohol compared to the control ($p= .014$) and placebo-alcohol primes ($p= .018$). However, there was no significant difference following the control prime compared to the placebo-alcohol prime ($p= .412$). Furthermore, there was no significant interaction between block and condition ($F (2, 66) = 1.28$, $p= .285$, $\eta_p^2= .04$). Lastly, a repeated measures ANOVA revealed a main effect of condition on incorrect responses in the no-signal blocks ($F (2, 54) = 14.24$, $p< .001$, $\eta_p^2= .30$). However, this revealed that participants made significantly more errors during the control session compared to the alcohol ($p< .001$) and placebo ($p< .001$) sessions, but no difference in errors between the alcohol and placebo sessions ($p= .525$).

Table 3: The number of incorrect responses shown separately for each block (no-signal, central stop-signal, peripheral stop-signal) of the SST and experimental condition (values are mean, SD).

	Control	Alcohol	Placebo
No-signal block	5.74 (3.66)	7.35 (5.31)	6.56 (6.24)
No-signal trials (central)	4.44 (2.94)	5.44 (5.05)	4.53 (4.61)
Stop-signal trials (central)	11.06 (2.91)	12.97 (3.52)	12.15 (2.54)
No-signal trials (periphery)	4.12 (3.01)	5.09 (4.51)	4.09 (3.54)
Stop-signal trials (periphery)	12.62 (4.53)	14.53 (5.23)	12.47 (3.74)

4.12 Chapter Summary

This chapter contributed to the overall aims of this thesis by replicating the findings of chapter 3 that heavy drinkers demonstrate proactive slowing, but also that the stopping process is influenced by the successful detection of stop-signals. Thus, this supports the suggestion that there is an *over-simplistic* conceptualisation of inhibitory control in the literature. However, although alcohol-cue exposure and alcohol intoxication increased alcohol-seeking, these results were unlikely due to impairments in inhibitory processes (reactive stopping, signal detection and proactive slowing). Indeed, there were only limited impairing effects of alcohol intoxication on reactive control, and neither intoxication nor alcohol-cue exposure impaired proactive slowing or signal detection. In particular, the results regarding the effect of alcohol-cue exposure on reactive control were surprising considering the seemingly robust impairing effect. This strengthened the rationale to clarify the role of proactive control and reactive control in heavy drinking, and to examine potential the mechanisms which may contribute to these effects.

CHAPTER 5

The associations between proactive slowing, working memory, alcohol sensitivity and alcohol use.

This chapter presents two online studies, the second of which was pre-registered on Open Science Framework (see Appendices 5), that were submitted as an original research article in the Journal of Studies on Alcohol and Drugs. The online supplementary materials are also presented after the article. Data for both studies is freely available on Open Science Framework (links are provided in main text). Task schematics are also presented in the Appendices (see Appendices 4 and 5). The format of the original article has been modified to match the other chapters in this thesis, however the content remains the same to that of which was submitted to the journal. To summarize contributions, I designed both studies which were approved by Andrew Jones. I collected the data with the help of second year undergraduate students. I analyzed the data and wrote the manuscript. Andrew Jones provided feedback on the manuscript before submission to the Journal of Studies on Alcohol and Drugs.

Chapter Foreword: This chapter contributed to the key aims of this thesis by further attempting to clarify the role of proactive slowing and reactive control in heavy drinkers, in the presence of alcohol-related cues. Due to the null findings in the laboratory thus far, these studies were conducted outside of the laboratory to increase sample sizes and ecological validity. Lastly, I also sought to examine potential mechanisms underlying the relationship between inhibitory processes and alcohol use. Specifically, I aimed to investigate the mediating effects of Working Memory Capacity in response to neutral-images and alcohol-related images, and also the mediating role of alcohol-sensitivity.

5.1 Abstract

Background**:* 'Reactive' inhibitory control is associated with heavy drinking and alcohol dependence. However, the majority of research ignores the downstream influence of proactive control – the preparation to withhold responses when examining alcohol-use behaviours. The potential mechanisms behind these relationships are also poorly understood. ***Objectives: These studies aimed to investigate the role of proactive and reactive control in heavy drinkers, in the presence of alcohol-related cues and to examine the potential mediating effects of Working Memory Capacity (WMC) and alcohol-sensitivity (AS). ***Methods:*** In two studies, heavy drinkers completed online self-reported measures of alcohol use followed by a modified Stop-Signal task in the presence of alcohol related cues (images – study 1; words – study 2) and a Self-Ordered Pointing Task using neutral-related images (study 1) and alcohol-related images (study 2). ***Results**:* In both studies, individual differences in proactive slowing and reactive control were not associated with individual differences in overall alcohol use. There was also no evidence that WMC or AS mediated the relationship between proactive slowing and alcohol use. However, poorer WMC was associated with increased alcohol use in study 1 and poorer proactive slowing in study 2. ***Conclusions/Importance:*** This study offers limited support for the associations between poorer WMC and increased drinking as well as poorer proactive slowing. However, individual differences in reactive control and proactive slowing were not associated with overall alcohol use, and these relationships were not mediated by WMC or AS.

5.2 Introduction

Inhibitory control is the (in)ability to inhibit behaviours that are inappropriate under current circumstances, and is closely linked to impulsivity and self-regulation (Baumeister, 2014; Bickel et al., 2012). The inability to inhibit incongruous behaviour has been associated with hazardous drinking (Christiansen, Cole, Goudie, et al., 2012; Houston et al., 2014; Paz et al., 2016)) and Alcohol Use Disorders (Smith et al., 2014). Inhibitory control is thought to fluctuate *within* individuals in response to various psychological and environmental triggers, including alcohol intoxication and alcohol-cue exposure (de Wit, 2009; Jones, Christiansen, et al., 2013), with these fluctuations playing a causal role in alcohol consumption/(re)lapse. Meta-analyses suggest small but robust impairments in inhibitory control following alcohol cue-exposure (Jones, Robinson, et al., 2018), however there are also failures to demonstrate this effect (Baines, Field, Christiansen, & Jones, 2019a; Jones, Rose, et al., 2013).

To date the majority of research in the field has focused on 'reactive' inhibitory control, which is the (unobservable) act of stopping or withholding a response, and is operationalized as inhibition errors/success or Stop-Signal Reaction Time (SSRT) on the Go/No-Go and Stop Signal tasks, respectively (Verbruggen, McLaren, et al., 2014). However, to effectively inhibit behavior requires a number of distinct downstream processes including action selection, the detection of an environmental signal to inhibit, and response execution, all of which may be influenced by proactive slowing (i.e. preparation) (Verbruggen, McLaren, et al., 2014). A failure to consider the role of preparation on these processes leads to *over simplistic* assumptions of the relationship between alcohol-related cues and inhibitory control. Indeed, Aron (Aron, 2011) suggests that proactive slowing may be a more appropriate model of inhibitory control in explaining real-world substance use behaviours. It seems more likely that individuals who are attempting to limit alcohol consumption will proactively adjust their behaviour to suppress urges over a prolonged period of time, rather than relying on fast, reactive inhibition that acts as a late correction mechanism (Braver, 2012; Braver et al., 2009).

Research suggests that alcohol-related cues may induce cognitive biases that influence proactive slowing and the execution of a reactive stopping response (Stacy & Wiers, 2010). Recent research has developed methods to disentangle proactive from reactive control, in order to separately measure their effects. Verbruggen et al (Verbruggen, Stevens, et al., 2014) incorporated a block of trials in which there was no inhibition signal on a Stop-Signal task (SST), and compared the reaction times on this block to a block of trials where inhibition was

required. The slowing of reaction times when inhibitory control is required (compared to not being required) is indicative of strategic proactive adjustments in control (Verbruggen & Logan, 2009b). In two recent studies (Baines et al., 2019a), we used a similar version of this task to examine if i) heavy drinkers employed proactive control and ii) if this was impaired by alcohol intoxication or exposure to alcohol-related cues. We demonstrated that heavy drinkers did utilise proactive control (i.e. they proactively slowed responses in anticipation of inhibiting), but there was limited impairing effects of alcohol intoxication or cue-exposure. These findings contrast previous research by Sharma (Sharma, 2017) who demonstrated that light drinkers proactively adjusted behaviour in response to alcohol-related cues in a Stroop task, whereas heavy drinkers relied on their reactive control as a late correction mechanism (see also (Braver, 2012)).

It is important to attempt to clarify the contrasting findings above, and one potential reason for these conflicting results is that the mechanisms underlying the preparation to inhibit responses are not well understood (Criaud et al., 2012). Theoretical models suggest that individual differences in Working Memory Capacity (WMC) might account for variance in the ability to implement both proactive and reactive control (Braver, 2012; Richmond et al., 2015). Individuals with greater capacity and more efficient WMC are more able to actively maintain goal-directed behaviour, by actively remembering and updating task rules (e.g. '*inhibition is (not) required at this time, under these circumstances'*) (Braver, 2012; Richmond et al., 2015). In support of this hypothesis, research has demonstrated that individuals with a high-WMC perform better than those with a low-WMC on the AX-Continuous Performance Test (e.g. (Redick & Engle, 2011; Wiemers & Redick, 2018)), a task which measures proactive and reactive control (Gonthier et al., 2016). Performance on this task has suggested that individuals with a lower-WMC tend to be less proactive than those with higher-WMC (Wiemers & Redick, 2018), and rely more on their reactive control (Richmond et al., 2015). Therefore, these studies support the notion that individual differences in the use of proactive control may depend on WMC. This could have important implications for understanding substance misuse as evidence suggests that both substance dependent individuals and heavy drinkers show impairments in WMC (Bechara & Martin, 2004; Mahedy et al., 2018; Noël et al., 2001).

Event-related potential (ERP) research has also demonstrated that alcohol-related stimuli capture the attention of individuals who self –report low sensitivity (LS) to alcohol (e.g. (Bartholow et al., 2010; Fleming & Bartholow, 2014)). These individuals have a low level of response to the acute effects of alcohol, which may lead to increased consumption of

alcohol per drinking session in order for the individual to experience the desired effects (Schuckit et al., 2011). A LS to alcohol is therefore considered a risk factor for alcohol misuse and dependence (Fleming & Bartholow, 2014; Schuckit & Smith, 2000). Alcohol sensitivity can be measured using self-report measure (discussed below) or by measuring blood alcohol concentration following a dose of alcohol (Schuckit et al., 2011). Importantly, it has been demonstrated that when LS individuals are faced with task irrelevant alcohol-related stimuli, they experience conflict. When conflict is infrequent, individuals can overcome it by using reactive control effectively, however, when this conflict increases, these individuals have difficultly using proactive control efficiently (Bailey & Bartholow, 2016). Therefore, it is possible that individual differences in alcohol sensitivity may contribute to the effective use of proactive and/or reactive control in the presence of alcohol-cue exposure.

Therefore, the aim of these two online studies was to clarify the role of proactive and reactive control in heavy drinkers, in the presence of alcohol-related cues (images – study 1, and words – study 2). We also sought to examine the potential mediating effects of WMC specifically in response to neutral images (study 1) and alcohol-related images (study 2), and also the mediating role of alcohol-sensitivity (study 2).[8] Study 1 was not pre-registered, however the design, statistical power calculations, hypotheses and analyses for study 2 were pre-registered on Open Science Framework [https://osf.io/ctp2w/]. Data is available for both studies on Open Science Framework [study 1; https://osf.io/4jkwd/ study 2; https://osf.io/j5hd3/].

5.3 Study 1

In this study heavy drinkers completed a modified SST (based on (Baines et al., 2019a)) designed to measure proactive slowing and reactive control in the presence of alcohol-related images. They also completed the Self-Ordered Pointing Task (SOPT) to measure their WMC and self-reported measures of alcohol consumption. We predicted that (i) individual differences in reactive control, proactive slowing and WMC would be associated with individual differences in overall alcohol use. We also predicted that (ii) individual differences in WMC would be associated with individual differences in proactive slowing and (iii) WMC would mediate the relationship between proactive slowing and alcohol use.

[8] In the pre-registration we did not specifically state that we would examine the mediating effects of WMC and AS. However, we believe this could add to the implications of the studies. We have labelled these sections of the results as exploratory.

5.4 Methods

5.4.1 Participants

Heavy drinkers (N=108; 82 female), with a mean age of 24.11 (±8.55) participated. The number of participants was decided upon using an a-prioi power calculation to detect a medium effect size (F^2 = .15) at α = .05, and 90% power with four predictors (craving, reactive control, proactive slowing, WMC). Participants were recruited via opportunity sampling from the university and wider community using social media and advertisements. Inclusion criteria were; aged 18+, heavy drinking (> 14 units per week) and access to a PC/laptop/Ipad. Exclusion criteria involved a current or previous diagnosis of alcohol dependence, determined via self-report. All participants provided informed consent before completing the study, which was approved by the University of Liverpool's Research Ethics Committee.

5.4.2 Materials

Questionnaires

The Timeline follow back (TLFB:(Sobell & Sobell, 1990)) was administered to measure retrospective alcohol consumption over the previous seven days in units (one UK unit = 8 g of alcohol). A visual guide providing the number of units in standard UK drinks was provided to assist participants in calculating their alcohol consumption. *The Alcohol Use Disorders Identification Test (AUDIT: (Saunders et al., 1993))* was also administered to measure hazardous drinking (study 1 α = .78; study 2 α = .78). Participants were asked when they last consumed alcohol (‘*When was the last time you drank alcohol?’* with the following options; more than one week ago, within the last week, in the last couple of days, yesterday, today, within the last couple of hours) (see (Jones & Field, 2015)). They were also asked about their motivation to reduce alcohol consumption (‘*On a scale of 0 (not at all) to 10 (extremely) how motivated are you to reduce your alcohol consumption?’*) and their current urge to drink alcohol (‘*What is your current craving for alcohol from 0 (no urge) to 10 (extreme urge)?’)* (or ‘*100 (extreme urge)?*’ in study 2). Lastly, participants were asked if they were distracted (‘*Were you distracted during the computer tasks?’* with the answers Yes or No). In both studies we included an attention check to ensure participants were paying attention as recommended for online research (Oppenheimer, Meyvis, & Davidenko, 2009), by including a question (*‘If you are paying attention leave this question blank’*: with the answers No, Yes but not in the last year and Yes during the last year) in the middle of the AUDIT.

Computer tasks

Modified Stop-Signal task (SST: (Verbruggen, Logan, & Stevens, 2008)

Participants completed a modified SST, which isolated proactive slowing and reactive control. On each trial, a letter ('X') or ('O') was displayed in the centre of the screen. Participants were asked to respond as fast and as accurate as possible to these 'go' stimuli. They were asked to press the left ('D') key with the left index finger if an ('X') was displayed and the right ('K') key with the right index finger if an ('O') was displayed. An alcohol-related image (e.g. a scene in a bar) appeared in the background on each trial. There were 10 of these images that were approximately 230 mm x 130 mm in size. Participants first completed a practice block of 10 trials (not recorded). The main task then consisted of two blocks:

No-signal block: In this block participants were asked to respond to the letters ('X' or 'O') without interruption on 100% of trials (N=40). Participants were informed that there would be no stop signals during this block.

Signal block: During this block, participants were asked to respond to the go-stimuli without interruption on 75% of trials (N=90). On the remaining 25% (N=30), two red lines "=" (stop-signal) appeared superimposed over the go stimulus. Participants were informed to attempt to inhibit their response if they saw this. The Stop-Signal Delay (SSD i.e. the delay between the presentation of the go stimulus and the stop signal) was adjusted on a trial-by-trial basis using a tracking procedure (Verbruggen & Logan, 2009a). The initial delay was 250 ms, if participants failed to inhibit the delay decreased by 50 ms making succeeding inhibition easier, if participants effectively inhibited then the delay increased by 50 ms making succeeding inhibition harder. Before starting the task, participants were also informed that they should respond as quickly as possible (i.e. not to wait for the stop-signal to appear) in line with standard SST instructions (Verbruggen et al., 2019).

Reactive control was inferred from SSRTs in the stop-signal block. This was calculated using the mean method (Verbruggen et al., 2013), which subtracts the mean SSD from the mean Go Reaction time on Go trials in the signal block (Go RT stop signal block-SSD). Proactive slowing was calculated by subtracting the mean reaction times for the no-signal block from the signal block ($RT_{stop\ signal} - RT_{no\ signal}$), with greater scores indicative of increased proactive slowing.

The Self-Ordered Pointing Task (SOPT: (Petrides & Milner, 1982)

Participants were shown a set of neutral images (e.g. couch, kettle) and asked to select one using the left hand mouse button. Following the selection of a picture, these were re-arranged into different positions. Participants were asked to try and avoid clicking the same picture more than once in a block and avoid clicking the same position in the array of images each time. Participants were first shown 6 images in a 2x3 array followed by 8-items in a 2x4 array, a 10-item block in a 2x5 array and finally a 12-item block in a 4x3 array. The number of trials in each block was in accordance with the number of images in the array. Participant's scores were displayed at the end of the task informing them of the number of errors made in each block (i.e. clicking on the same image more than once) and the total number of errors. The total number of errors was used as a measure of WMC. Task schematics are presented on OSF [https://osf.io/ucwj4/].

5.4.3 Procedure

The study was completed using Inquisit Web 5.0 (Millisecond software). Participants were first presented with an information sheet and gave informed consent. Next, they completed the SST followed by the SOPT in a counterbalanced order. Participants then gave demographic information and completed the questionnaires. Lastly, participants were debriefed and thanked for participation. The session took approximately 10-15 minutes to complete, and participants could opt in to a prize draw for £50 in high street vouchers.

5.4.4 Data reduction and analysis

A composite measure of alcohol use was computed as our dependent variable. This was used as in previous research (see (Baines, Jones, & Christiansen, 2016; Christiansen & Bloor, 2014; Fernie et al., 2013)) to capture a better picture of the general pattern of alcohol use rather than specific behaviours such as binge drinking. The overall measure of alcohol use consisted of the units consumed (measured by the TLFB), scores on the AUDIT and the frequency of heavy episodic drinking days (6+ units in a single session for females, 8+ for males (Office for National Statistics, 2018)), z-scored and combined. We ran a Principal Component Analysis, which confirmed that total AUDIT scores, units consumed, and heavy days drinking loaded onto a single component (eigenvalue = 2.25; accounting for 77.48% of variance with all factor loadings $\geq .74$). In line with previous research (Jones & Field, 2015),

we also removed participants from the analyses if they self-reported consuming alcohol on the same day of testing (study 1: n = 8; study 2: n = 7), to ensure that inhibitory control and working memory were not affected by acute alcohol intoxication. For the SST, outliers were removed following criteria suggested in previous research (Field, Kiernan, Eastwood, & Child, 2008). Reaction times that were greater than 2000ms or less than 100ms were removed; as were reaction times that were greater than 2.5 standard deviations above the individual mean score. We also removed any SSRTs which were negative, in line with previous research (Congdon et al., 2012). We used a similar method for the SOPT (Thush et al., 2008) in that the total scores which were greater than 2.5 standard deviations above the mean score were removed. Three participants failed the attention check; however removal of these did not significantly alter the interpretation of our results.

5.5 Results

5.5.1 Sample characteristics (see table 1)

There were no significant differences between males and females in AUDIT scores (t (98) = -.360, p= .720, d= -0.07), heavy drinking days (t (98) = 0.09, p= .929, d= 0.02) or TLFB scores (t (28) = 1.52, p= .140, d= 0.57). There were also no significant differences in craving scores (t (98) = 1.86, p= .067, d= 0.38) or motivation to reduce alcohol consumption (t (98) = 0.02, p= .983, d= 0.00).

5.5.2 The associations between individual differences in reactive control, proactive slowing, WMC and overall alcohol use (see table 2).

We conducted a multiple regression analysis to investigate if individual differences in SSRTs, craving, proactive slowing and WMC predicted individual differences in overall alcohol use. Variance inflation factors (VIF) ranged between 1.14 and 1.21 suggesting there were no issues with multi-collinearity. The overall model predicted approximately 19% of variance (R^2= .19; F (4, 94) = 5.39, p< .001). Increased craving for alcohol was associated with increased overall alcohol use (β= .25, p= .013, 95% CI .06 to .46). WMC (β= .26, p=.010, 95% CI .04 to .29) also significantly predicted overall alcohol use with increased errors on the SOPT being associated with higher alcohol use (see fig 1 in Supplementary materials). However, neither SSRTs (β= -.01, p= .940, 95% CI -.01 to .01) nor proactive slowing (β= .10, p= .342, 95% CI -.00 to .01) were significant predictors of alcohol use.

Table 2: Descriptive statistics and Pearson's correlations for overall alcohol use, craving, reactive control, proactive slowing and working memory.

	Mean (SD)	2	3	4	5
Overall alcohol use	0.00 (2.58)	.33*	.11	.11	.34*
Craving	2.00 (2.50)	-	.16	.05	.33*
SSRTs	287.51 (69.85)	-	-	.37*	.15
Proactive slowing	125.83 (141.84)	-	-	-	-.02
Working memory	6.18 (4.10)	-	-	-	-

*Overall alcohol use = units consumed (measured by the TLFB), scores on the AUDIT and the frequency of heavy episodic drinking days (6+ units in a single session for females, 8+ for males; (Office for National Statistics, 2018)), z-scored and combined. Craving = 0 (no urge for alcohol) to 10 (extreme urge for alcohol). SSRTS = reactive control. Higher scores = worse reactive control. Higher Proactive slowing = better proactive slowing. Working memory = errors on SOPT. Higher scores = worse working memory. *p<.01*

5.5.3 Exploratory Analyses

We also aimed to investigate whether individual differences in WMC mediated the relationship between proactive slowing and overall alcohol use. However, although WMC significantly predicted overall alcohol use, there was no association between individual differences in WMC and proactive slowing (see table 2; p= .867). Therefore, we did not meet the assumptions required to examine mediation.

5.6 Interim discussion

Study 1 demonstrates that increased craving and poorer working memory were associated with increased overall alcohol use in a sample of heavy drinkers. However, individual differences in neither proactive slowing nor reactive control did not significantly predict individual differences in overall alcohol use or WMC.

Table 1: Descriptive statistics for AUDIT scores, TLFB scores, heavy drinking days, craving scores and motivation to reduce alcohol consumption, split by gender in Study 1 and Study 2 (values are mean (SD)).

	Study 1			Study 2		
	Males (n=22)	Females (n=78)	Sample (N=100)	Males (n=49)	Females (n=60)	Sample (N=109)
AUDIT	10.00 (5.59)	10.50 (5.81)	10.39 (5.73)	13.51 (6.20)	12.55 (6.20)	12.98 (6.19)
TLFB	24.77 (19.59)	17.95 (14.53)	19.45 (15.93)	43.73 (28.51)	29.13 (19.60)	35.70 (24.99)
Heavy drinking days	1.41 (1.30)	1.38 (1.10)	1.39 (1.14)	2.18 (1.81)	2.35 (1.71)	2.28 (1.75)
Craving	2.86 (2.98)	1.76 (2.31)	2.00 (2.50)	17.49 (22.54)	16.25 (21.89)	16.81 (22.09)
Motivation	2.59 (2.91)	2.58 (2.62)	2.58 (2.67)	2.59 (2.41)	2.53 (1.91)	2.56 (2.14)

AUDIT=Total scores on the AUDIT. TLFB = Total units reported in the TLFB. Heavy drinking days = occurrences of heavy episodic drinking days in the 7-day TLFB (Study 1) and 14-day TLFB (study 2) (6+ units in a single session for females, 8+ for males; (Office for National Statistics, 2018)). Craving = 0 (no urge) to 10 (extreme urge) or 100 (extreme urge; study 2). Motivation to reduce alcohol consumption = 0 (not at all) to 10 (extremely).

5.7 Study 2

In study 2, participants completed a SST in which they responded directly to alcohol-related words (rather than ambiguous letters) in order to increase alcohol cue-reactivity. They also completed a SOPT in which they had to remember alcohol-related stimuli (rather than neutral-related stimuli), and completed a questionnaire assessing their alcohol sensitivity. We predicted that (i) individual differences in proactive slowing, reactive control, WMC and alcohol sensitivity would be associated with individual differences in overall alcohol use. We also predicted that (ii) individual differences in WMC would be associated with individual differences in proactive slowing and (iii) individual differences in alcohol sensitivity would predict the ability to implement proactive slowing and reactive control. Lastly, we hypothesised that (iv) WMC and AS would mediate the relationship between proactive slowing and alcohol use.[9]

5.8 Methods

5.8.1 Participants

Heavy drinkers (N=116; 63 female), with a mean age of 22.01 ($\pm$6.09) were recruited from the university and wider community using social media and advertisements. The number of participants was decided upon using a power calculation to find a medium effect size (F^2 = .15) at α = .05, and 90% power with five predictors (craving, reactive control, proactive slowing, working memory, alcohol sensitivity). The inclusion and exclusion criteria were identical to those described in study 1.

5.8.2 Materials

Computer Tasks

Modified Stop-Signal task (Verbruggen, Stevens, et al., 2014)

Participants also completed a modified SST, which isolated proactive slowing and reactive control. On each trial participants were shown a white horizontal line (approximately 70 mm) in the middle of the screen for 500ms. An alcohol-related word (e.g. 'beer') then appeared either above or below the line. If the word appeared above the line, participants pressed one key ('T'), if the word appeared below the line, participants pressed another key

[9] We did not pre-register this hypothesis. Therefore it is labelled as exploratory in the results section.

('V') using the keyboard (these 'keys' appeared at the bottom on the screen on touch screen devices). A neutral word (e.g. 'sponge') also appeared simultaneously but participants were asked not to respond to this. These were no-signal trials. We chose the words based on those used in previous research which developed matched alcohol and control words, specifically (Cox, Brown, & Rowlands, 2003). There were 10 generic alcohol-related words (beer, vodka, shorts, whiskey, bar, alcopops, stout, cocktails, spirits, alcohol) and 10 generic neutral-related words (brush, duster, polish, squeegee, shammy, shampoo, sponge, flannel, bucket, hoover). On stop-signal trials, the white line turned red and participants were told to try and withhold their response when this occurred. The blocks, stop-signal probability, tracking procedure and calculations of proactive/reactive control were the same described in study 1.

Modified Self-Ordered Pointing Task (Petrides & Milner, 1982)

This task was identical to the task described in study 1. However, instead of neutral images participants completed the task using alcohol-related images (e.g. pint of beer, glass of wine). Task schematics are presented on OSF [https://osf.io/fybgv/].

Questionnaires

The questionnaires administered were identical to that of study 1, except the TLFB was administered for fourteen days instead of seven to capture a better picture of individuals' drinking patterns. Additionally, participants also completed *The Alcohol Sensitivity Questionnaire (ASQ:* (Fleming et al., 2016)) (α = .94). This included 15 items asking participants how many alcoholic drinks they must typically drink to experience alcohol-related effects. Specifically, 9 of these items are associated with lower doses of alcohol and stimulation (e.g. increasing talkativeness) and 6 are associated with heavier doses of alcohol and sedation (e.g. passing out). Participants were first asked whether or not they have experienced each alcohol-related effect and if the answer was YES, they were asked to estimate the minimum number of drinks required to experience the lower dose effects or the maximum number of drinks they could consume without experiencing the higher dose effects. The total score is the number of drinks stated with higher scores on this questionnaire indicating low sensitivity to alcohol.

5.8.3 Procedure

The procedure is identical to that described in study 1.

5.8.4 Data Analysis

The data was handled using identical procedures to those in study 1. We computed the same overall measure of alcohol use. We ran a Principal Component Analysis which confirmed that total AUDIT scores, units consumed (measured by the TLFB) and heavy drinking days loaded onto a single component (eigenvalue = 2.07; accounting for 68.97% of variance with factor loadings of .64 to .93). Additional details regarding this and the analysis of each hypothesis can be found in the pre-registration on Open Science Framework. However, for the ASQ we calculated a composite score as missing data has previously been shown to result in biased ASQ scores. Therefore we used the standardized person mean imputation approach (Bailey & Bartholow, 2016; Lee et al., 2015). We first standardised ASQ scores by transforming these into z-scores and then calculated the mean score across all non-missing items. On average participants answered 11.69 (± 2.86) questions, which is a similar average reported in previous research (e.g. Mean = 11.40 (Bailey & Bartholow, 2016)). This procedure was not pre-registered, however it provides more robust data estimates. Ten participants did not fully complete the SST and these were removed from the analysis. Three participants failed the attention check; however removal of these did not significantly affect results.

5.9 Results

5.9.1 Sample characteristics (see table 1)

There was no significant difference between males and females in AUDIT scores (t (107) = 0.81, p = .423, d= 0.16) or heavy drinking days (t (107) = -0.49, p= .623, d= -0.09). There were also no significant differences in craving (t (107) = 0.29, p= .772, d= 0.06) or motivation to reduce alcohol consumption (t (91) = 0.14, p= .890, d= 0.03). However, males did consume significantly more units than females (t (82) = 3.05, p= .003, d = 0.67).

5.9.2 The associations between individual differences in proactive slowing, reactive control, WMC, alcohol sensitivity and overall alcohol use (see table 3).

We conducted a multiple regression analysis to investigate if individual differences in SSRTs, proactive slowing, WMC and alcohol sensitivity predicted individual differences in overall alcohol use. Variance inflation factors (VIF) ranged between 1.00 and 1.08 suggesting there were no issues with multi-collinearity. The overall model predicted approximately 13% of variance (R^2= .13; F (5, 89) = 2.74, p =. 024). Increased craving (β= .25, p= .014, 95% CI

.01 to .05) was a significant predictor of increased alcohol use. However, SSRTs (β= -.19, p= .066, 95% CI -.01 to .00), proactive slowing (β= .03, p= .747, 95% CI -.00 to .01), working memory (β= -.06, p= .593, 95% CI -.21 to .12), and alcohol sensitivity (β= .18, p= .073, 95% CI -.06 to 1.34) were not significant predictors of overall alcohol use.

5.9.3 Exploratory Analyses

We also aimed to investigate whether individual differences in WMC/AS mediated the relationship between proactive slowing and overall alcohol use. However, although poorer WMC predicted poorer proactive slowing, there was no relationship between overall alcohol use and WMC or AS (see above). AS was also not related to proactive slowing (see table 3; p= .540). Therefore, we did not meet the assumptions required to examine mediation.

Table 3: Descriptive statistics and Pearson's correlations for overall alcohol use, craving, reactive control, proactive slowing, working memory errors and alcohol sensitivity.

	Mean (SD)	2	3	4	5	6
Overall alcohol use	0.00 (2.53)	.21*	-.16	.07	-.09	.13
Craving	16.81 (22.09)	-	-.04	-.03	-.05	.06
SSRTs	340.05 (101.90)	-	-	-.13	.04	-.01
Proactive slowing	15.24 (102.29)	-	-	-	-.24*	-.06
Working memory errors	5.07 (3.27)	-	-	-	-	.09
Alcohol sensitivity	0.02 (0.70)	-	-	-	-	-

*Overall alcohol use = units consumed (measured by the TLFB), scores on the AUDIT and the frequency of heavy episodic drinking days (6+ units in a single session for females, 8+ for males; (Office for National Statistics, 2018)) ,z-scored and combined. Craving = 0 (no urge for alcohol) to 100 (extreme urge for alcohol). SSRTS = reactive control. Higher scores = worse reactive control. Higher Proactive slowing = better proactive slowing. Working memory = errors on SOPT. Higher scores = worse working memory. Alcohol sensitivity = composite measure of Alcohol sensitivity. Higher scores = lower sensitivity to alcohol. *p<.05. See fig 2 in supplementary materials illustrating the relationship between proactive slowing and working memory errors.*

5.10 Discussion

The current studies investigated if individual differences in reactive control and proactive slowing were associated with individual differences in overall alcohol use in heavy drinkers. We also aimed to investigate if WMC and AS mediated the relationship between the proactive slowing and overall alcohol use. However, contrary to our predictions neither individual differences in proactive slowing nor reactive control were associated with individual differences in overall alcohol use in either study. Although poorer working memory was associated with increased alcohol use in study 1, it was unrelated to the ability to implement proactive slowing and the opposite relationship was observed in study 2. Individual differences in AS were also unrelated to alcohol use or proactive slowing in study 2. Therefore there was no evidence that WMC or AS mediated the relationship between proactive slowing and alcohol use.

These findings support models (e.g. (Verbruggen, McLaren, et al., 2014)) which suggest that investigating reactive inhibition only is of limited theoretical benefits. We were able to isolate proactive slowing and reactive control in both studies. However, we failed to replicate studies that have demonstrated a relationship between reactive control and alcohol use (e.g. (Christiansen, Cole, Goudie, et al., 2012; Colder & O'Connor, 2002; Paz et al., 2016)), thus finding limited empirical support for models of addiction which posit inhibitory control as a candidate mechanism of action (e.g. (de Wit, 2009; Fillmore, 2003; Goldstein & Volkow, 2002)). It is still plausible that a relationship exists between proactive slowing and alcohol use, however, it is also possible that the relationship between inhibitory control and alcohol use has been over-emphasised or is influenced by publication bias and small study effects. There are numerous studies which have reported null findings (e.g. (Czapla et al., 2015; Fernie et al., 2010; Nederkoorn et al., 2009)). Furthermore, an updated meta-analyses by Smith et al (Smith & Mattick, 2018) suggested that inhibitory deficits are not associated with heavy drinking. Continuing well-powered and pre-registered studies should begin to correct any biases in the literature and elucidate the true nature of the relationship.

We demonstrated some support for research that has shown WMC is associated with alcohol use in study 1 (e.g. (Mahedy et al., 2018; Peeters et al., 2015; Thush et al., 2008)). However this relationship did not exist in the presence of alcohol-related cues (study 2). We also found limited support for the relationship between WMC and the ability to implement proactive slowing (e.g. (Richmond et al., 2015; Wiemers & Redick, 2018)). This relationship may have useful real-world implications i.e. high-WMC individuals may have an increased

ability to initiate and maintain goals (in this case response selection) compared to low-WMC individuals (Richmond et al., 2015). Furthermore, we failed to replicate studies that have demonstrated that alcohol sensitivity is associated with increased risk for heavy drinking (Fleming & Bartholow, 2014), or associated with the ability to implement proactive slowing (Bailey & Bartholow, 2016).

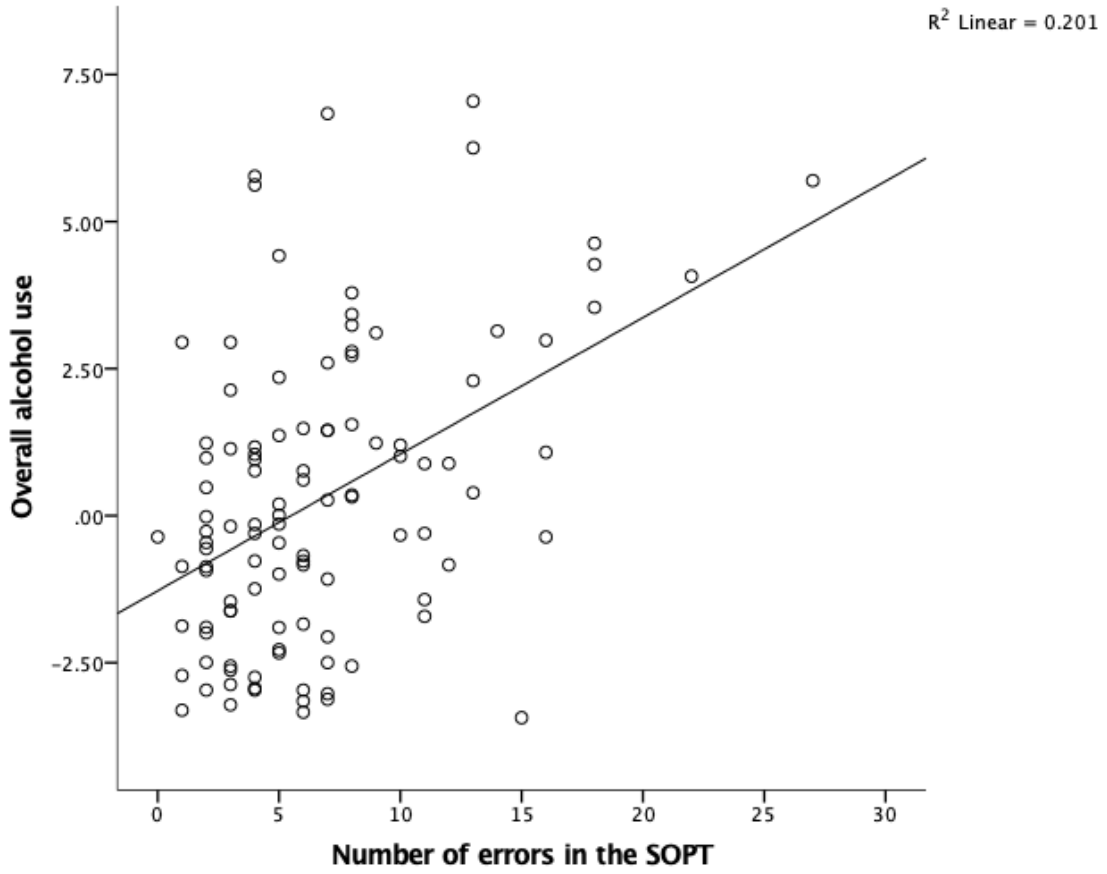
These studies have limitations. We used a cross-sectional design and therefore we are unable to investigate these relationships over time. Furthermore, in study 1 there was an over-representation of females, thus future research should aim to recruit a more representative sample. Lastly, 32 participants in study 1 and 34 in study 2 stated that they were distracted during the computer tasks and 11 participants in study 2 also did not answer this question (see supplementary materials for sensitivity analysis; correlations between working memory and alcohol use (study 1) and proactive slowing (study 2) were no longer significant). The proportion of reported distractions are similar to recent Ecological Momentary Assessment studies examining SST and alcohol consumption in the real word (Jones, Tiplady, Houben, Nederkoorn., & Field., 2018). However, completing these tasks online in the participant's natural environment rather than in the laboratory does increase the ecological validity of the study, as in the real world inhibition occurs in 'noisy' surroundings (Verbruggen, Stevens, et al., 2014). Furthermore, only three participants in both studies responded incorrectly to the attention measure in the AUDIT and removal of these did not significantly affect results. Lastly, the current studies only sought to examine proactive slowing. However, it is also possible to measure proactive inhibition (rather than slowing) by incorporating a cue into the Stop-Signal tasks (Verbruggen & Logan, 2009b). This cue informs participants about the likelihood of a stop-signal occurring and therefore this index of inhibition could also provide a useful avenue for future research.

In conclusion, we have demonstrated no evidence that inhibitory control processes (reactive and proactive) are associated with alcohol use in non-dependent drinkers. Furthermore, we demonstrated no convincing evidence for our proposed mediators of WMC or alcohol sensitivity. Given the increasing number of null findings, it is possible the role of inhibitory control in alcohol use has been overemphasised.

5.11 Supplementary Information

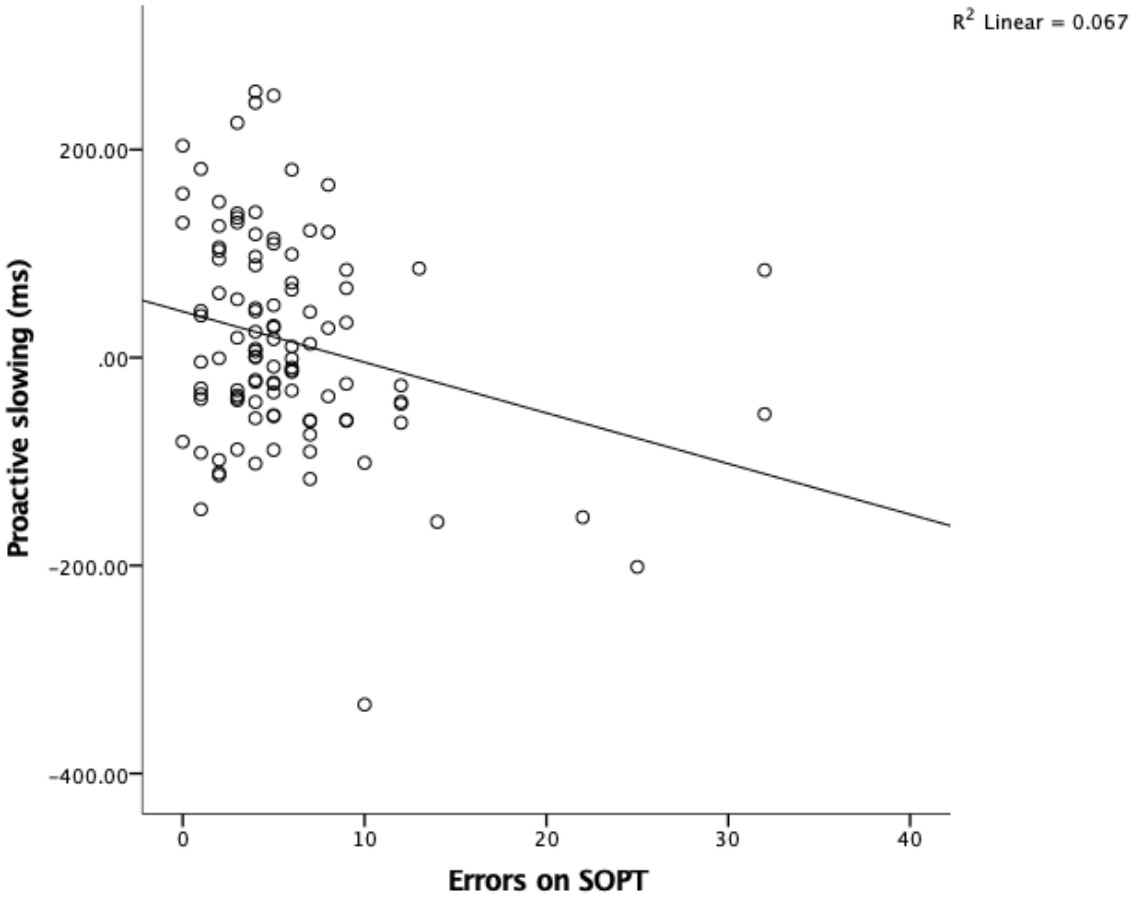
5.11.1 Study 1 Results

Supplementary Fig 1: A scatterplot to show the relationship between errors on the SOPT (Working Memory Capacity) and overall alcohol use.



5.11.2 Study 2 Results

Supplementary Fig 2 A scatterplot to show the relationship between individual differences in Working Memory Capacity (errors on the SOPT) and proactive slowing.



Distraction measure

In both studies we asked participants whether they were distracted during the computer tasks. In study 1, 32 participants reported that they were distracted. Removal of these removed the association between working memory and overall alcohol use, however this may have been caused by a reduction in statistical power. In study 2, 34 participants stated that they were distracted during the computer tasks and 11 failed to answer the question. Removal of these had no effect on the multiple regression. However, when examining correlations, the relationship between working memory and proactive slowing was no longer significant. This again may have been due to a reduction in statistical power.

5.12 Chapter Summary

This chapter contributed to the overall aims of this thesis by adding support to suggest that inhibitory control is comprised of both reactive and proactive control, and that there is an *over-simplistic* conceptualisation of inhibitory control in the literature. However, there were no associations between individual differences in reactive or proactive control and alcohol use in heavy drinkers. As this has been a common finding in this thesis so far, this strengthens the rationale to examine neurophysiological responses of inhibitory control in the following chapter, which may offer a more sensitive investigation into these relationships (and the fluctuations in inhibitory processes), compared to behavioural data. Lastly, there was also some evidence for the suggestion that individual differences in WMC may underlie the effective use of proactive control. This supports the rationale to examine this potential mechanism in a laboratory setting in the following experimental chapter.

CHAPTER 6

The effect of acute stress and alcohol-related cues on proactive and reactive inhibitory control.

This chapter presents a laboratory study which has been prepared for publication. The supplementary materials are also presented. This study was pre-registered on Open Science Framework (see Appendices 6) (link is provided in text). To summarize contributions to this chapter, I designed the study which was approved by Andrew Jones. I collected and analyzed the data with the assistance of Nick Fallon. I wrote the manuscript and Andrew Jones provided feedback on this.

Chapter Foreword: Due to the limited findings reported in the previous chapters, this chapter contributed to the overall aims of this thesis by providing a more sensitive investigation into fluctuations in inhibitory processes. Specifically, this study aimed to investigate the effect of acute stress on the behavioural indexes (proactive inhibition, proactive slowing, SSRTs) and the neurophysiological components (P300, N200) of inhibitory control, in the presence of alcohol-related cues, in heavy drinkers. I also aimed to investigate whether impairments in the behavioural indices or neurophysiological responses following acute stress were associated with increased alcohol seeking. Lastly, I found limited evidence for the potential mechanisms (Working Memory Capacity, alcohol sensitivity), which may underlie effective proactive slowing in the previous online studies. Thus, I sought to investigate these in a laboratory environment.

6.1 Abstract

Background*:* Inhibitory control is suggested to be a state variable, which fluctuates in response to environmental and psychological triggers. However, little research has investigated the effect of these triggers on proactive inhibitory processes. ***Objectives:*** This pre-registered study aimed to investigate whether acute stress impaired proactive and reactive inhibitory control, lead to neurophysiological changes in the P300 and N200 Event-Related Potentials (ERPs) in the presence of alcohol-related cues, and increased alcohol-seeking. ***Methods:*** Forty heavy drinkers attended two laboratory sessions on a within-subjects basis, in which they either completed an easy set of anagrams (control) or were asked to prepare a presentation on their physical appearance (stress). Participants then completed a Working Memory (Self-Ordered Pointing) task, and a modified Stop-Signal task whilst their electrophysiological responses were recorded, followed by an *ad libitum* taste test. ***Results:*** Acute stress had limited effects on reactive stopping, and had no effect on proactive inhibitory processes or the neurophysiological correlates of response inhibition. Contrastingly, alcohol-cue exposure did impair proactive stopping and increase P300 responses (compared to neutral-cues). Lastly, although proactive stopping was associated with *ad libitum* alcohol consumption following acute stress, there was no evidence of a relationship between inhibitory processes (or neurophysiological responses) and alcohol consumption. We also found limited evidence for the mechanisms underlying these effects. ***Conclusions/Implications:*** These results offer limited support to models that suggest inhibitory control is a state variable that fluctuates in response psychological and environmental triggers. Certainly, there was little evidence of a relationship between inhibitory processes and *ad libitum* alcohol consumption.

6.2 Introduction

Inhibitory control - the (in)ability to control inappropriate behaviour in certain situations-is suggested to fluctuate *within* individuals in response to multiple internal and situational triggers, including alcohol-cue exposure, alcohol intoxication and stress (de Wit, 2009; Jones, Christiansen, et al., 2013). This may have important implications for addiction interventions since research has demonstrated that poor inhibitory control predicts the transition from heavy drinking to dependence (Rubio et al., 2008), comorbid drug and alcohol use (Nigg et al., 2006) and treatment success/risk of relapse (Rupp et al., 2016).

Notably, evidence has exposed short-term impairments in inhibitory control following alcohol-cue exposure in non-dependent drinkers (e.g. (Jones & Field, 2015; Muraven & Shmueli, 2006; Petit et al., 2012)), and meta-analyses have suggested that this effect is small but robust (Jones, Robinson, et al., 2018), although there have been some discrepancies (e.g. (Baines et al., 2019a; Jones, Rose, et al., 2013)). There is also some contradictory evidence with regards to the acute effects of stress on inhibitory control with some research demonstrating impairments (Roos et al., 2017; Scholz et al., 2009; Starcke et al., 2016; Zack et al., 2011), whilst others have revealed enhanced inhibitory performance following acute stress (Constantinou et al., 2010; Schwabe et al., 2013) or null findings (McGrath et al., 2016). Consequently, there has been a suggestion that the effect of stress on inhibitory control may be in accordance with a U-shaped function, with a moderate level of stress improving performance but a high or low level of stress impairing performance (see (Henderson et al., 2012)).

However, one possible explanation for these contradictory findings is the focus on 'reactive' inhibitory control (outright stopping), indexed by Stop-Signal Reaction Time (SSRT) in Stop-Signal tasks or commission errors in Go/No-Go tasks, despite cognitive neuroscience models (e.g. (Verbruggen, McLaren, et al., 2014)) suggesting that this is an *over-simplistic* conceptualization of inhibitory control. Certainly, research has suggested that although reactive control is useful, successful response inhibition is also the result of preparation through the use of proactive control (Criaud et al., 2012). This involves preparation to withhold a response in anticipation of a stop-signal rather than relying on outright stopping in response to the presentation of a stop-signal (Aron, 2011; Castro-Meneses et al., 2015). As such, this may provide a more appropriate explanation of substance use (Aron, 2011). It is more likely that substance users would proactively adjust their behaviour over time to control their cravings rather than relying on outright stopping of their

drinking behaviour through a late correction mechanism (Braver, 2012; Braver et al., 2009). Importantly, proactive and reactive control can be isolated and have been measured using modified Stop-Signal tasks (SST) in previous research (e.g. (Baines et al., 2019a; Baines, Field, Christiansen, & Jones, 2019b; Verbruggen & Logan, 2009b; Verbruggen, Stevens, et al., 2014)). However, there is still limited evidence investigating proactive control in the addiction literature.

Another possible explanation for contradictory findings is the reliance on behavioural measurements (e.g. response times, accuracy) in the literature. These measurements can be volatile and influenced by a variety of factors (e.g. hardware delays (Woods et al., 2015) or past experience of similar tasks (Wong et al., 2017)). As an alternative, neurophysiological evidence may offer a more sensitive investigation into the effect of stress and alcohol-cue exposure on inhibitory control processes. In support of this, Dierolf et al (Dierolf, Fechtner, Böhnke, Wolf, & Naumann, 2017) reported that acute stress did not damage response times or response accuracy on a Go/No-Go task, however it did impact the neural correlates of response inhibition. Specifically, acute stress was found to increase difference waves of the Event-Related Potential (ERP) P300 but decrease the ERP N200. Ceballos et al (Ceballos, Giuliano, Wicha, & Graham, 2012) also reported that stress increased N200 amplitudes (but had no effect on P300 amplitudes) in social drinkers. As such, the N200 and P300 ERPs have been associated with two aspects of inhibitory control (Enriquez-Geppert et al., 2010; Huster et al., 2013; Liu et al., 2015). Specifically, the P300 is thought to represent the final stages of an inhibitory response (reactive control: (Wessel & Aron, 2015)), whereas the functional specificity of the N200 component still has a degree of uncertainty (Dimoska et al., 2006) with the possibility it is related to response conflict or error monitoring (Donkers & van Boxtel, 2004; Enriquez-Geppert et al., 2010; Kok et al., 2004; Yeung et al., 2004). For example, participants may experience conflict when they have to over-ride a frequent pre-potent response to respond, when presented with infrequent no-go stimuli or a stop-signal (Braver, Barch, Gray, Molfese, & Snyder, 2001). This can be manipulated by altering the frequency of responses required (Enriquez-Geppert et al., 2010).

Indeed, the N200 is a negative component which peaks around 200-250ms following presentation of a stop-signal, whereas the P300 is a positive component which peaks after the N200 (at around 300-350ms following a stop-signal) (Dimoska et al., 2003; Jones, Field, et al., 2013). When response inhibition is successful, the P300 component has been shown to consistently increase in amplitude more than when inhibition is unsuccessful, whereas the N200 ERP has been shown to have larger amplitudes during failed inhibition (Dimoska et al.,

2003; Jones, Field, et al., 2013; Kok et al., 2004). Importantly, evidence has suggested that reduced P300 amplitudes during response inhibition could be a marker for vulnerability to alcohol dependence (Hesselbrock et al., 2001; Kamarajan et al., 2005). Furthermore, in the laboratory Jones et al (Jones, Field, et al., 2013) demonstrated that individual differences in amplitudes of P300 subcomponents during response inhibition were negatively associated with alcohol intake during an *ad libitum* taste test.

ERPs may also be modulated by salient cues. A meta-analysis (Littel, Euser, Munafo, & Franken, 2012) of studies with various task paradigms (e.g. passive, oddball paradigms) also showed that those with substance dependence exhibit increased P300 amplitudes in response to substance-related cues (compared to neutral-cues) and that this effect is larger compared to healthy controls (standardised mean differences 0.61 vs. 0.22). This has also been demonstrated in heavy, non-dependent drinkers (Herrmann et al., 2001). Contrastingly, evidence has also demonstrated decreased N200 components following exposure to alcohol-cues (compared to neutral-cues) in non-dependent drinkers or differences in N200 and/or P300 components between light drinkers and heavy drinkers when exposed to alcohol-related cues during inhibitory control tasks (Kreusch et al., 2014; Petit et al., 2012; Watson et al., 2016). Thus, further examination of these components following acute stress and/or alcohol-cue exposure may contribute to our understanding or inhibitory control as a state variable.

Finally, a last reason for contradictory evidence may be due to the poor understanding of the mechanisms underlying the preparation for response inhibition (Criaud et al., 2012). Research has suggested that individuals with a low sensitivity to alcohol are at risk for heavy drinking and alcohol misuse (Fleming & Bartholow, 2014). This is because these individuals may consume more alcohol per drinking session to experience the desired effects as they have a low level of response to the effects of alcohol (Schuckit et al., 2011). Importantly, research has suggested that these individuals experience increased conflict when trying to inhibit responses to alcohol-cues (Fleming & Bartholow, 2014), and have difficulty implementing proactive control when faced with frequent alcohol-related cues (Bailey & Bartholow, 2016). Other ERP research has demonstrated increased P300 amplitudes in individuals with a low sensitivity to alcohol in response to alcohol-related cues (Bartholow, Henry, & Lust, 2007; Bartholow et al., 2010). Therefore, it is plausible that individual differences in alcohol sensitivity may contribute to the efficient use of proactive control when exposed to alcohol-cues.

Lastly, varied amplitudes of P300 have also been related to WMC (Saliasi, Geerligs, Lorist, & Maurits, 2013) and stress has also been shown to impair working memory

performance (e.g. (Luethi, Meier, & Sandi, 2008; Oei, Everaerd, Elzinga, van Well, & Bermond, 2006; Schoofs, Preuss, & Wolf, 2008)). This is unsurprising considering working memory processes are thought to support behavioural control (Finn, 2002) or inhibitory mechanisms are subsumed under WMC in some models (Miyake & Friedman, 2012). Indeed, research has suggested that individual differences in WMC may explain variance in the ability to effectively use proactive and reactive control (Braver, 2012; Richmond et al., 2015), with supporting evidence demonstrating that individuals with a high-WMC perform better and are more proactive than those with a lower WMC on tasks such as the AX-Continuous Performance Test (e.g. (Redick & Engle, 2011; Wiemers & Redick, 2018)). Further evidence regarding this could contribute to addiction interventions as research has demonstrated that both heavy drinkers and those with substance dependence show deficits in WMC (Bechara & Martin, 2004; Mahedy et al., 2018; Noël et al., 2001).

Consequently, this study aimed to investigate whether acute stress impaired proactive and reactive control and lead to changes in the amplitudes of P300 and N200 ERPs during inhibitory control. We aimed to investigate whether these impairments occurred only in the presence of alcohol-related cues, since research has showed that acute stress significantly increases attentional biases towards alcohol-related cues (e.g. (Field & Powell, 2007; Field & Quigley, 2009)) and that alcohol-related cues cause state fluctuations in 'reactive' inhibitory control (Jones & Field, 2015; Jones, Robinson, et al., 2018; Petit et al., 2012). We also aimed to investigate if acute stress lead to increased alcohol consumption (compared to a control condition) and if deficits in proactive control, reactive control and the neurophysiological correlates of inhibitory control were related to individual differences in alcohol consumption. We included the alcohol-seeking measures as experimental evidence has demonstrated that acute stress increases subjective craving for alcohol (Field & Powell, 2007) and *ad libitum* alcohol consumption in heavy drinkers (McGrath et al., 2016). Lastly, we aimed to examine the potential mechanisms (i.e. WMC and AS) underlying the preparation of responses. The design, hypotheses, power calculation and analyses were pre-registered on Open Science Framework (https://osf.io/s2utw/).

6.3 Method

In this study, heavy drinkers completed a control session and a session in which they were subject to a psychological stressor. During both sessions, they also completed a modified SST (based on (Baines et al., 2019a)), designed to measure reactive and proactive control, whilst

their electrophysiological responses were measured. Participants also completed a Self-Ordered Pointing Task to measure their WMC and an *ad-libitum* taste test. It was hypothesised that (i) acute stress would cause deficits in reactive stopping, proactive stopping and proactive slowing in the presence of alcohol-related cues. It was also predicted that (ii) participants would consume more beer (as a % of total fluid) following acute stress (compared to control) and that (iii) impairments in proactive and reactive control would predict unique variance in alcohol consumption. Furthermore, we predicted that (iv) acute stress would lead to differences in the magnitude of P300 and N200 responses in the presence of alcohol-cues (compared to control) and that (v) the magnitude of these responses to alcohol-cues would be associated with individual differences in alcohol consumption. Finally, it was hypothesised that (vi) AS would be associated with the ability to implement proactive and reactive control and individual differences in the amplitudes of P300 in response to alcohol-cues and that (vii) acute stress would impair WMC (compared to control) with WM performance associated with the ability to implement proactive control, P300 amplitudes and *ad libitum* alcohol consumption.

6.3.1 Participants

Heavy drinkers (N= 40; 17 male), with a mean age of mean age 24.70 ($\pm$ 10.39) were recruited from the University of Liverpool and wider community to take part in a two-session laboratory study. An a-priori power calculation was used to decide upon the number of participants required to find a medium effect size based on previous studies which have examined the effect of stress or alcohol-cues on inhibitory control (e.g. (Czapla et al., 2015; Dierolf et al., 2017; Kreusch, Vilenne, & Quertemont, 2013; Scholz et al., 2009) (dz = .50, at α = .05, 1-β = 90%). Inclusion criteria were heavy drinking (>14 units per week based on UK Government guidelines), aged 18+, a fluent English speaker and a self-reported motivation to reduce alcohol consumption. Exclusion criteria included a current or previous self-reported diagnosis of ADHD, a psychiatric disorder, or alcohol dependence. Participants were also excluded from taking part if they were suffering from any illness (or taking medication) that could increase sensitivity to alcohol-related effects, were pregnant or currently breastfeeding. All participants gave informed consent before taking part in the experiment, which received approval from The University of Liverpool Research Ethics Committee.

6.3.2 Materials

Questionnaires

Participants completed baseline measures of their alcohol consumption and personality. This included a *Timeline follow back* (TLFB: (Sobell & Sobell, 1990)) to measure the quantity of alcohol (units) consumed in the two-weeks prior to taking part in the study (one UK unit = 8g of alcohol) and the *Alcohol Use Disorders Identification Test* (AUDIT: (Saunders et al., 1993)) to measure hazardous drinking (α = .56). Participants also completed *The Alcohol Sensitivity Questionnaire* (ASQ; (Fleming et al., 2016)) to measure average alcohol consumption required to experience alcohol-related effects, including effects associated with lower doses of alcohol and stimulation (e.g. feeling socially at ease or increased talkativeness) and higher doses and sedation (e.g. vomiting or passing out). Low sensitivity to alcohol is indicated through a higher number of drinks recorded (α's > .81). We computed a composite score for the ASQ (see (Bailey & Bartholow, 2016; Lee et al., 2015)) as although not pre-registered, this prevents bias in the data from missing scores and therefore provides a more robust estimate for responses. To do this, we transformed items to z-scores and then calculated the mean across all non-missing items. Participants answered an average of 10.61 (±3.02) which is similar to previous literature (Bailey & Bartholow, 2016).

The Brief Comprehensive Effects of Alcohol Questionnaire ((CEOA-B; (Ham et al., 2005)) was also administered to measure alcohol outcome expectancies (α's > .85) and the *Temptation and Restraint Inventory* (TRI: (Collins & Lapp, 1992)) to measure drinking restraint (α's > .53). Additionally, three subscales of self-reported craving (Inclined/Indulgent, Obsessed/Compelled, Resolved/Regulated) were also measured using the *Approach and Avoidance of Alcohol Questionnaire* 'right now' version (AAAQ; (McEvoy et al., 2004)) at the beginning of the study and after the computer tasks (α's > .65).

To measure impulsivity, participants completed the *Barratt Impulsivity Scale* (BIS: (Patton et al., 1995)) (α's > .76). The 'trait' items of the *State-trait Anxiety Inventory* (STAI; (Spielberger et al., 1999)) were administered to measure trait anxiety at the beginning of the study (α = .95). The 'state' items were administered to measure current feelings of anxiety i.e. 'right now' at the beginning of the study, after the stress manipulation and at the end of the session (α's > .89). This has been used to measure stress in previous studies (e.g. (Field & Powell, 2007; Field & Quigley, 2009; Starcke et al., 2016)). At the end of the second session, participants were also required to answer an open question to assess their awareness of the

overall experimental aims of the study and three fixed-response questions to assess their awareness specifically of the presentation task, the Stop-Signal task and the taste test.

Computer tasks

Modified Stop-Signal task (SST; (Baines et al., 2019a))

Participants completed a modified SST to measure proactive inhibition, proactive slowing and reactive control (see fig 1 in Appendices 6 for task schematic). This was programmed using PsychoPy version 2. At the start of each trial, a small fixation cross was presented in the centre of the screen for 1000ms. After this, an alcohol-related image (e.g. someone taking a drink of beer or wine) or a neutral-related image (e.g. people in an office appeared). Participants were told they should use their right hand to press the 'V' key if the image was alcohol-related or the 'N' key if the image was neutral-related as quickly as possible. These were no-signal trials. There were 10 alcohol-related images and 10 neutral-related images that were approximately 180 mm x 100 mm in size. A practice block of 20 trials were first completed to ensure participants understood the instructions. Two main task blocks then followed in a counter-balanced order:

No-signal block: Within this block, participants were asked to respond to the images (alcohol-related or neutral-related) without interruption on 100% of trials as quickly as possible (N=40).

Stop-signal block: Within this block, participants were asked to respond to the images on 50% of trials (N=320). On the other half of trials (N=320), a stop-signal was presented in the form of two red lines "=" that appeared in the centre of the image. Participants were told to try and withhold their response when this occurred but were also given standard stop-signal instructions that they should respond as quickly as possible and not wait for the stop-signal to appear (Verbruggen et al., 2019). To aid this, participants were informed that the fixation cross at the beginning of each trial may sometimes turn red and this indicated that the requirement for response inhibition was more likely. If the fixation cross was white, participants were informed that the requirement for response inhibition was less likely.

Specifically, participants completed 240 no-signal trials with no inhibition cue (N=120 alcohol-related images; N=120 neutral-related images), 80 no-signal trials with an inhibition cue (N=40 alcohol-related images; N=40 neutral-related images), 80 trials with a stop-signal and no inhibition cue (N=40 alcohol-related images; N=40 neutral-related images), and 240 trials with a stop-signal and cue (N=120 alcohol-related images; N=120

neutral-related images). Therefore, participants were required to withhold their response on 25% of trials with no prior information and 75% of trials with prior information. The Stop-Signal Delays (SSD) were fixed at 200ms, 300ms and 400ms. As this increased the percentage of stop-signal trials from the standard 25%, a break was inserted after every 100 trials asking participants to wait for the experimenter to check the electrodes before re-starting and they were reminded of their instructions not to wait for the stop-signal to appear, as this has been shown to reduce the reliability of SSRTs (Verbruggen et al., 2019).

Proactive slowing was inferred from the degree of reaction time slowing on the stop-signal block compared to the no-signal block (Median RTstop signal − Median RTno signal). Higher scores indicated increased proactive slowing. Proactive stopping was inferred from the proportion of inhibitory failures on the cued stop-signal trials in the signal block (as these involve preparation of responses). Reactive control was inferred from SSRTs in the stop-signal block. These were computed using the integration method[10] (Logan & Cowan, 1984) as the SSDs were fixed. Using this method, SSRTs are estimated by subtracting the SSD from the finishing time of the stopping process. Thus, SSRTs are estimated for each SSD separately and then averaged (Verbruggen & Logan, 2009a). The effects of stress on each process were then measured by comparing performance across conditions (control, stress).

Modified Self-Ordered Pointing Task (SOPT; (Petrides & Milner, 1982))

This task was programmed using Inquisit 5.0 Lab. Participants were shown a set of 12 alcohol-related images in a 4 x 3 array (e.g. a pint of beer, a glass of wine) and asked to click a picture using the left-hand mouse button. The pictures then re-arranged and a new trial began where participants were required to select a different picture again. They were required to do this 12 times per block (N=3 blocks). Participants were told to try and avoid clicking any of the pictures more than once during each block and were also told that they could not click the same position each time. Once completed, the number of errors for each block and the total number of errors were displayed (i.e. the number of times participants clicked the same images). The total number of errors was used as a measure of WMC, with a higher score indicating poorer WMC (see fig 2 in Appendices 6 for task schematic).

[10] The mean method was stated in the pre-registration. However, the integration method is thought to be more reliable and less biased, particularly when using fixed stop-signal delays (Verbruggen et al., 2019).

Stress manipulation

In the control session, participants were given 100 easily solvable anagrams and were asked to solve as many as they could for 5 minutes. They were informed they could attempt these in any order and if they were stuck they should move on. In the stress condition, participants were instructed to prepare a 5-min presentation on the topic '*what I dislike about my body and physical appearance.'* This was based on previous research (e.g. (Field & Powell, 2007; Gullo & Stieger, 2011; McGrath et al., 2016)) and a meta-analysis (Dickerson & Kemeny, 2004) which showed that physiological stress is robustly increased by exposure to social evaluative threat. Participants were informed that this activity was to assess their personality and that the experimenter would stay to watch them present their speech but that it would also be recorded on a video camera and assessed by a trainee clinical psychologist on the basis of organisation, articulation, openness and defensiveness. Participants were given a pen and some paper to prepare for five minutes and were told that they would deliver their presentation at the end of the experiment. Whilst the participant prepared, the experimenter set up a video camera on a tripod stand and informed the participants that they were attaching the camera now so that the participant could get used to it, but it would not start recording until the participant presents their speech at the end of the session.

Ad libitum taste test

Participants were simultaneously provided with 500ml of chilled Skol beer (2.8% vol. ABV) and 500ml of chilled fresh orange juice (non-alcoholic beverage) in non-branded glasses. Participants were asked to taste and rate the drinks on various gustatory dimensions e.g. '*How pleasant was drink 1?'* using Visual Analogue Scales and were instructed to '*drink as much or as little as you like in order to make accurate judgements.'* This procedure has demonstrated good construct validity (Jones, Button, et al., 2016). Before beginning, participants were also informed that after completion they would take part in a final cognitive task, in which they could potentially win small monetary prizes, but that alcohol has been shown to impair performance on this task. This was to increase participants' motivation to control their alcohol intake during the bogus taste test (Baines et al., 2019a; Christiansen et al., 2013; Field & Jones, 2017). However, participants only actually completed the task during session one as performance was of secondary importance here. After the participant had left the laboratory, the volume of each beverage consumed was recorded. The measure of

ad libitum alcohol consumption was calculated as the volume of beer consumed as a percentage of total fluid consumed.

6.3.3 Procedure

Participants attended two counterbalanced laboratory sessions at The University of Liverpool between 12:00-18:00pm, separated by at least one week. At the beginning of the first session participants were informed that the experiment was investigating the associations between cognitive processes, personality differences and the taste perception of alcohol. They were first breathalysed and a recording of 0.00mg/l was required to take part. Participants then completed their demographic information followed by the baseline measures of self-reported alcohol consumption, personality, stress, and alcohol craving. Depending on condition, participants then completed the control task (the list of anagrams) or the stress task (presentation task) followed by the 'state' items of the STAI to measure stress post-manipulation. The cognitive tasks (modified-SST and SOPT) were then completed in a counter-balanced order. Before completing the modified-SST, participants were fitted with the appropriately sized electrode cap and were moved into a sound attenuated chamber. They were seated approximately 150 cm away from the computer display and were asked to use their right hand only to respond during the task. They were also informed that they should only blink when the fixation cross was presented on the screen. Breaks were presented between blocks where the experimenter checked on the participant and after every 100 trials in the stop-signal block.

After completing the task, the electrode cap was removed and participants were given the opportunity to wash the gel out of the hair at the end of each session. Following the cognitive tasks, participants completed the AAAQ to measure craving followed by the *ad libitum* taste test and the BART (first session only). The 'state' items of the STAI were then completed to check feelings of stress at the end of the session and participants were breathalysed before they left the laboratory.

Upon returning for the second session, participants were breathalysed to ensure they had a reading of 0.00mg/l. They then completed the AAAQ and the 'state' items of the STAI. Following this, participants completed the counterbalanced stress or control task and the 'state' items of the STAI. The cognitive tasks were then completed with the electrode cap re-fitted before completion of the modified-SST, followed by the AAAQ, the *ad-libitum* taste test and the 'state' items of the STAI. Lastly, participants completed the awareness of

experimental aims questionnaire and were breathalysed and debriefed before leaving the laboratory. There was also the option of a cool down period provided at the end of the stress session where they could remain in the laboratory and discuss the study.

EEG recording

The Biosemi ActiveTwo electrode system (Biosemi B.V, Amsterdam, Netherlands) was used to record continuous EEG activity. The recording bandpass filter was 0.16 to 100 Hz with a sampling rate of 512 Hz. Participants were fitted with a 64-electode cap. Four flat-type active electrodes were also fitted above, below and to the right of the right eye and to the left of the left eye to measure electrooculograms (EOG movements) to measure muscle movements.

6.3.4 Data reduction and analysis.

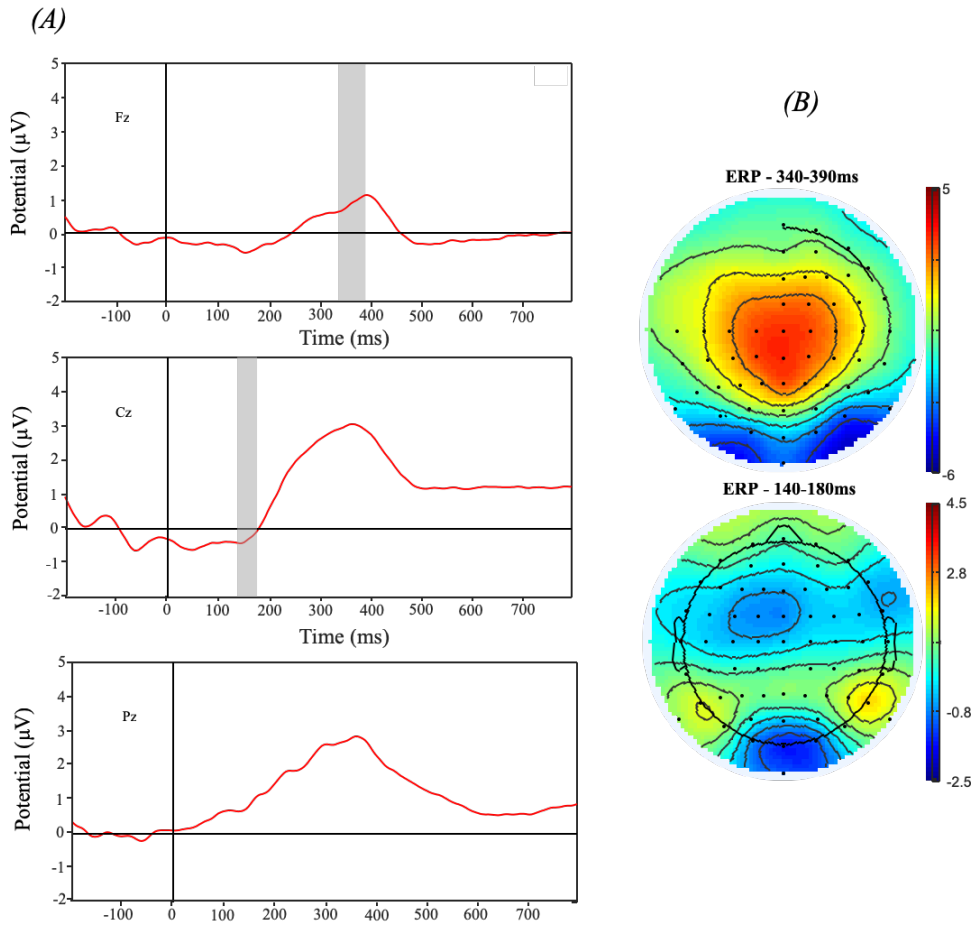
Information regarding the analyses can be found on Open Science Framework (see Appendices 6). In line with previous research (Congdon et al., 2012), we removed any negative SSRTs. We also removed any reaction times that were >2000ms or <100ms or more than 2.5 standard deviations above the individual mean score in line with past literature (Field et al., 2008). Two participants were removed due to a technical error/failing to respond, these were also removed from the EEG analysis. In the SOPT, we followed similar guidelines to past research (Thush et al., 2008) and removed total errors that were more than 2.5 standard deviations above the mean score. One participant was removed as data did not record for one session. Lastly, one participant was removed from the BAC analysis due to a technical issue with a breathalyser.

With regards to the neurophysiological data, electroocular and electrocardiographic artifacts were removed using Principal Component Analyses (Berg & Scherg, 1994). Data were visually inspected for the presence of movement or muscle artifacts in Brain Electrical Source Analysis (BESA) version 7.0, and epochs contaminated with artifacts were manually excluded in Matlab v.8.10 (The Mathworks Inc, Natick, MA). EEG data was filtered with a high pass filter (0.5 Hz) and low pass filter (45 Hz). ERP's were epoched (averaged) according to onset of the stop-signal in each of the conditions. The Epochs lasted from -200 before the stop-signal to 800 ms after presentation of the stop-signal. Baseline data correction was performed using the data -200 to 0 ms relative to stop-signal. Visual inspection Grand average (all subjects and all conditions) ERP data, butterfly plots and surface topographies were used to identify the centre of time windows representing the peak times for occurrence

of components of interest. The largest positive peak after presentation of the stop-signal was inferred as the P300. This is in line with past research (e.g. (Jones, Field, et al., 2013; Kamarajan et al., 2005)). This peaked around 365 ms in a window of 340-390 ms after the stop-signals. The N200 was then inferred as the first negative peak that occurred before the P300. This was found by observing the data backwards and peaked at around 160ms, occurring between 140-180 ms following the stop-signals. In line with past research (Jones, Field, et al., 2013; Kamarajan et al., 2005), midline electrodes (Pz, Fz and Cz) were used to investigate differences in P300 and N200 amplitudes (see fig 1).

Six participants were removed due to technical issues with the EEG recording equipment (i.e. poor signal, issues with triggers recording). Lastly, to ensure there was no differences in the percentages of trials removed from the analysis between conditions, a 2 (condition: control, stress) x 2 (image: alcohol, neutral) x 2 (cue: no-cue, cue) repeated measures ANOVA was also conducted on the percentage of stop-signal trials included. This revealed no main effects of condition ($F (1, 32) = 0.39$, $p= .536$, $\eta_p^2 = .01$), image ($F (1, 32) = 0.004$, $p= .948$, $\eta_p^2 = .00$) or cue ($F (1, 32) = 2.50$, $p= .124$, $\eta_p^2 = .07$ and no significant interactions ($ps > .05$).

Fig 1: (A) A comparison of ERPs along the midline electrodes (Fz, Cz, and Pz). (B) The topographic maps indicate the mean voltage topography across whole scalp during these time windows.



Grand average waveforms at electrode Cz (all subjects, all conditions combined) were used to select the time periods for P3 and N2 components. The grey bars indicate the time selected (P3 = 340-390 ms, N2 = 140-180 ms).

6.4 Results

6.4.1 Sample Characteristics (see table 1)

Table 1 demonstrates that the sample were characteristic of heavy drinkers. Independent samples t-tests revealed no significant difference between males and females in AUDIT

scores (t (38) = 0.95, p= .349, d= .30) or units consumed [11]prior to taking part (t (21) = 1.37, p= .187, d= .46). There were also no significant differences in trait anxiety scores between males and females (t (38) = -.35, p= .728, d= -0.11).

Table 1: Sample characteristics based on baseline measures taken at the beginning of the study, shown separately for males and females (values are mean, SD).

	Sample (N=40)	Males (n=17)	Females (n=23)
AUDIT scores	12.70 (4.41)	13.47 (4.94)	12.13 (3.99)
TLFB Units	42.99 (25.43)	49.94 (34.02)	37.85 (15.48)
STAI -Trait	44.05 (12.50)	43.24 (12.83)	44.65 (12.51)

Note: TLFB Units = Alcohol units consumed 14 days prior to taking part measured using a Timeline follow back (1 UK unit = 8g of alcohol). STAI Trait = Total scores on the Trait version of the State Trait Anxiety Inventory (scored between 20-80).

6.4.2 Manipulation check (stress) (see table 2)

A 2 (condition: control, stress) x 3 (time: pre-manipulation, post-manipulation, end of session) repeated measures ANOVA was conducted on the State items of the STAI. This revealed a significant main effect of condition (F (1, 39) = 9.27, p= .004, η_p^2=.19) with scores higher in the stress condition compared to the control condition. There was also a significant main effect of time (F (2, 64) = 38.47, p< .001, η_p^2= .50) with scores significantly higher at post-manipulation compared to pre-manipulation (p<.001) and end of session (p<.001). There was no significant difference between pre-manipulation and end of session (p= .374). Lastly, there was also a significant condition * time interaction (F (2, 78) = 7.48, p= .001, η_p^2= .16). Post hoc LSD tests demonstrated that scores increased from pre-manipulation to post-manipulation in both the stress (p<.001) and control (p<.001) conditions, however scores at post-manipulation were significantly higher in the stress condition compared to the control condition (p<.001), suggesting the manipulation was successful in increasing stress. There were no significant differences between conditions at pre-manipulation (p= .816) or end of

[11] TLFB data was not normally distributed and therefore was log transformed to try and improve the distribution. However, this did not alter the results of the t-test and therefore non-transformed data is presented.

session after participants had been informed they would not complete the presentation (p= .107).

Table 2: Average scores on the State version of the STAI at pre-manipulation, post-manipulation and end of session (values are mean, SD).

	Pre-manipulation	Post-manipulation	End of session
Control Condition	33.03 (10.49)	36.43 (10.66)	31.38 (7.48)
Stress Condition	33.33 (9.17)	43.15 (13.71)	33.73 (8.87)

6.4.3 Behavioural results (see table 3).

Deficits in reactive control were investigated using a 2 (condition; control, stress) x 2 (image; alcohol, neutral) x 2 (cue; no-cue, cued) [12]repeated measures ANOVA on SSRTS in the signal block. There was no main effect of condition (F (1, 36) = 3.80, p= .059, η_p^2 = .10) or image (F (1, 36) = 1.22, p= .276, η_p^2 = .03). The main effect of cue was significant (F (1, 36) = 24.56, p< .001, η_p^2 = .41), showing that contrary to expectations, SSRTs were significantly faster in response to no-cue trials compared to cued trials. Furthermore, there was a significant condition * cue interaction (F (1, 36) = 5.62, p= .023, η_p^2 = .14). This showed that for cued trials, SSRTs were significantly faster in the control session compared to the stress session (p= .011), but there was no difference for no-cued trials (p= .346). Furthermore, SSRTs were significantly faster for no-cued trials (compared to cued trials) in both the control (p= .009) and the stress (p< .001) sessions. There were no other significant interactions (ps>.05).

Impairments in proactive stopping were also investigated using a 2 (condition; control, stress) x 2 (image; alcohol, neutral) x 2 (cue, no cue) repeated measures ANOVA on the proportion of inhibition errors in the signal block on stop-signal trials. This revealed no main effect of condition (F (1, 37) = 1.19, p= .282, η_p^2 = .03) suggesting stress did not impair proactive stopping. However, there was a main effect of image (F (1, 37) = 7.67, p= .009, η_p^2 = .17) with an increased number of errors made for alcohol images compared to neutral images. There was also a main effect of cue (F (1, 37) = 22.24, p< .001, η_p^2 = .38) with more

[12] This Independent Variable was incorrectly missed from the pre-registration.

inhibition errors made for no-cue trials compared to cued trials. There were no significant interactions (ps > .05).

Lastly, a 2 (condition; control, stress) x 2 (block; no-signal, signal) x 2 (image; alcohol, neutral) repeated measures ANOVA was conducted on no-cue go reaction times to measure deficits in proactive slowing. Due to an uneven number of trials in the no-signal block and the no-cue trials in the stop-signal block, we computed median RTs rather than means. There was no main effect of condition (F (1, 37) = 0.01, p= .923, η_p^2 = .00) suggesting stress did not impair proactive slowing. However, there was a main effect of block (F (1, 37) = 139.08, p< .001, η_p^2 = .79) with participants slowing down their responses in the stop-signal block compared to the no-signal block. There was also a main effect of image (F (1, 37) = 25.19, p< .001, η_p^2 = .41) with participants responding significantly faster to alcohol-related images compared to neutral-related images. There were no significant interactions (ps > .05).

Table 3: Descriptive statistics for SSRTs (reactive stopping), inhibition errors (proactive stopping) (values are mean, SD), and median go-reaction times (ms) (values are median, SE) shown separately for each condition and image

	Control		Stress	
	Alcohol	Neutral	Alcohol	Neutral
SSRT (no-cue)	286.87 (55.12)	281.76 (48.08)	294.77 (88.28)	294.11 (64.07)
SSRT (cued)	307.82 (56.49)	304.65 (82.84)	340.02 (62.93)	328.95 (88.07)
Inh. Errors (no-cue)	9.05 (7.34)	8.38 (7.25)	12.03 (16.48)	10.47 (14.66)
Inh. Errors (cued)	6.13 (6.49)	5.00 (5.98)	8.42 (15.44)	7.70 (15.11)
NS block RT	600.26 (18.90)	650.35 (18.59)	600.82 (17.29)	629.07 (20.76)
SS block RT (no-cue)	760.68 (16.84)	780.54 (20.73)	740.53 (17.54)	767.18 (18.87)

Beer consumption

A paired samples t-test was conducted to measure beer consumed (as a percentage of total fluid) in the *ad libitum* taste test. However, this revealed no significant difference between

beer consumed in the control condition and the stress condition (t (39) = -0.46, p= .645, d= .05; see table 4 and table 5 for descriptive statistics). There was also no significant difference in mean BAC's at the end of the control condition (0.04 ±0.06) compared to the stress session (0.05 ±0.07; t (38) = -0.50, p= .617, d= .15).

Working Memory Capacity

A paired samples t-test demonstrated no significant difference in the total number of errors made in the SOPT during the control condition and stress condition; t (36) = 0.06, p= .950, d=.01; see table 4 and table 5 for descriptive statistics).[13]

6.4.4 Neurophysiological results (see fig 2)

P300

A 2 (condition: Stress vs No-Stress) x 2 (image: Alcohol vs Neutral) x 2 (cue: no-cue, cue) x 3 (Electrode: Fz, Cz, Pz) repeated measure ANOVA was conducted on P300 mean amplitudes to investigate differences following stress. This revealed no main effect of condition (F (1, 30) = 2.24, p= .145, η_p^2 = .07) or cue (F (1, 30) = 0.59, p= .447, η_p^2 = .02). However, there was a main effect of image (F (1, 30) = 7.10, p= .012, η_p^2 = .19), which showed that mean amplitudes were significantly higher for alcohol-related images compared to neutral-related images. There was also a main effect of electrode (F (2, 47) = 17.31, p< .001, η_p^2 = .37), which demonstrated that amplitudes of the Fz electrode were significantly smaller compared to the Pz electrode (p= .001) and the Cz electrode (p< .001) but there was no difference between amplitudes in the Pz and Cz electrodes (p= .412). Lastly, there was significant condition * cue (F (1, 30) = 4.57, p= .041, η_p^2 = .13) and image * electrode (F (2, 60) = 4.69, p= .013, η_p^2 = .14) interactions. These revealed that amplitudes for alcohol-related images were significantly higher than neutral-related images for the Cz electrode. Furthermore, for both alcohol-related and neutral-related images, amplitudes were significant lower for Fz electrodes compared to Pz (p= .001) and Cz (p< .001) electrodes. However, there were no other significant differences (ps > .05).

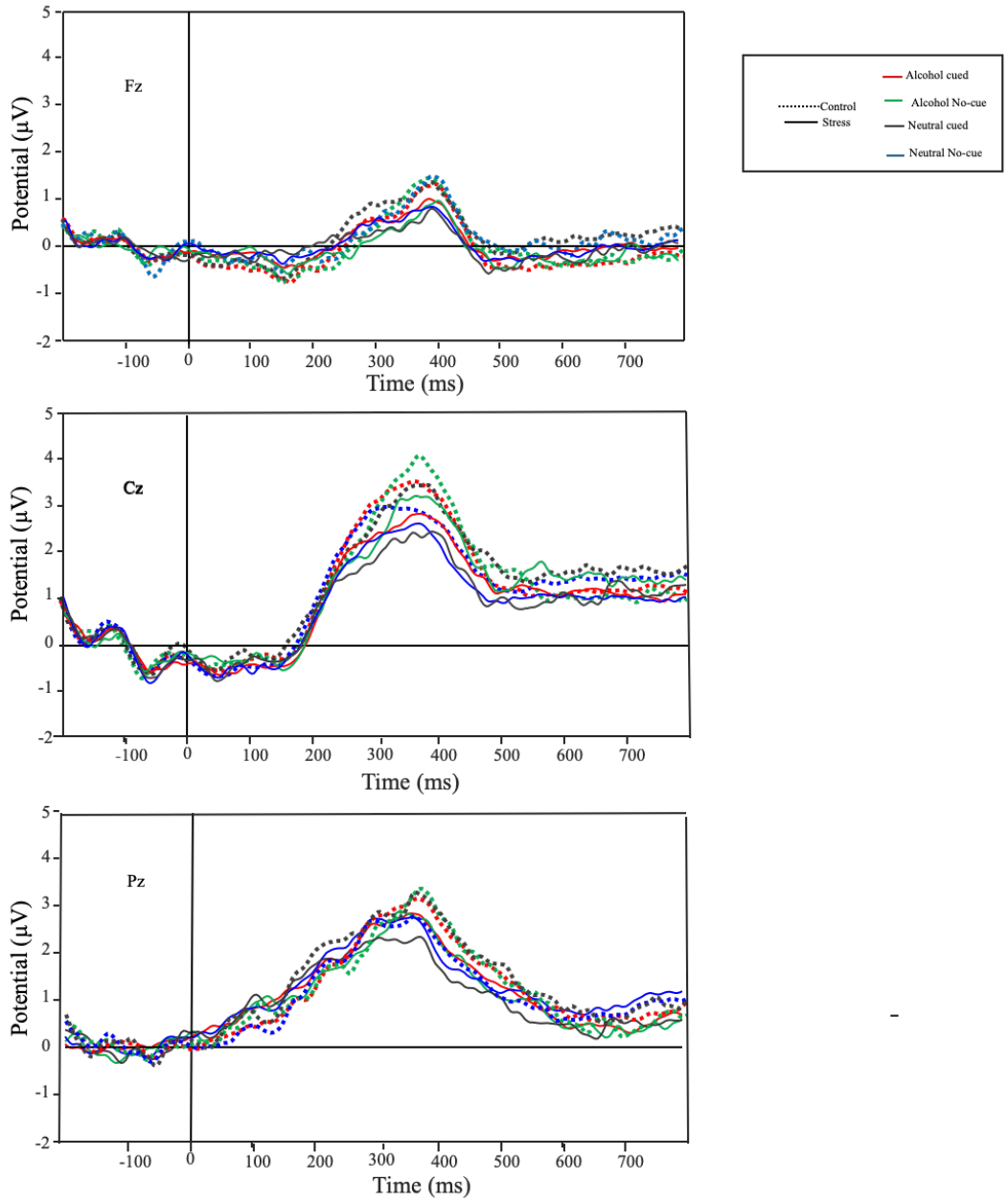
[13] Data was skewed and therefore log transformed. However, the result was still non-significant and therefore the non-transformed data is presented here. Outlier analysis was also performed but removing these had no effect upon results.

N200

A 2 (condition: Stress vs No-Stress) x 2 (image: Alcohol vs Neutral) x 2 (cue: no-cue, cue) x 3 (Electrode: Fz, Cz, Pz) repeated measures ANOVA was also conducted on N200 mean amplitudes. This revealed no main effect of condition (F (1, 32) = 0.05, p= .832, η_p^2 = .001), image (F (1, 32) = 0.26, p= .613, η_p^2 = .01) or cue (F (1, 32) = 1.47, p= .234, η_p^2 = .04). However, there was a main effect of electrode (F (2, 64) = 32.00, p< .001, η_p^2 = .50), which revealed significantly higher amplitudes for the Pz electrode compared to the Fz (p< .001) and Cz electrodes (p< .001). There was no difference between mean amplitudes for the Fz and Cz electrodes (p= .210). There was also no significant interactions (ps > .05).

We also hypothesised that following acute stress, impairments in proactive and reactive control, and the magnitude of N200/ P300 responses to alcohol-cues, would predict unique variance in alcohol consumption. However as there was no difference in alcohol consumption between sessions, these analyses are reported in the supplementary materials. Table 4 and 5 also presents correlation matrices to show the associations between AS and WMC with inhibitory processes, neurological responses and *ad libitum* alcohol consumption.

Fig 2: A comparison of ERP components along midline electrodes (Fz, Cz and Pz) for each condition (control, stress).



6.5 Discussion

The current studies aimed to investigate if exposure to acute stress and alcohol-cues impaired reactive and proactive control, and lead to changes in the neurophysiological responses of inhibitory control. We also sought to investigate if these impairments/changes were predictive of increased alcohol consumption in an *ad libitum* taste test or related to potential mechanisms that could underlie these relationships. The behavioural results showed that there

was limited effects of acute stress on reactive stopping and no effect on proactive processes. There was also no effect of alcohol-cue exposure on reactive stopping or proactive slowing, however exposure to alcohol-cues did impair proactive stopping (as indicated by increased inhibition errors) compared to neutral-cue exposure. Poorer proactive stopping was also moderately associated with increased *ad libitum* alcohol consumption following exposure to acute stress (see table 4). However, acute stress did not significantly increase *ad libitum* alcohol consumption, and impairments in reactive stopping or proactive slowing did not predict increased alcohol consumption.

These findings offer limited support for theoretical models (de Wit, 2009; Jones, Christiansen, et al., 2013) that suggest impairments in inhibitory control fluctuate in response to psychological (acute stress) and environmental (alcohol-cue exposure) triggers. Certainly, the finding that acute stress did not impair reactive stopping contrasts previous research (Roos et al., 2017; Scholz et al., 2009; Starcke et al., 2016), although there have been other 'null' findings (e.g. (McGrath et al., 2016)). However, the condition * cue interaction did demonstrate that stress impaired reactive stopping to cued stop-signal trials. Nevertheless, we hypothesised that the impairing effect of stress would be in response to alcohol-related cues only, thus our findings also contradict research which has demonstrated that acute stress increases attentional biases towards alcohol-related cues (Field & Powell, 2007; Field & Quigley, 2009), and impairs 'reactive' control following exposure to alcohol-related cues (Zack et al., 2011).

Indeed, alcohol-cue exposure also had no effect on reactive stopping. This contradicts research that has demonstrated short-term impairments in inhibitory control following alcohol-cue exposure (e.g. (Muraven & Shmueli, 2006; Petit et al., 2012; Weafer & Fillmore, 2012)). However, Jones et al's meta-analyses (Jones, Robinson, et al., 2018) reported this effect to be small in magnitude (standardised mean difference 0.21) and we found similar results in a previous study (Baines et al., 2019a), with others also reporting discrepancies (e.g. (Jones, Rose, et al., 2013; Nederkoorn et al., 2009)). Indeed, alcohol-cue exposure did impair proactive stopping, but there is a paucity of literature to compare this finding to. It could be interpreted that this finding supports Sharma (Sharma, 2017), who also demonstrated how heavy drinkers had difficulty implementing proactive control in a modified Alcohol-Stroop task, and were instead relying on reactive stopping as a late correction mechanism (Braver, 2012).

The null finding with regards to alcohol-seeking following acute stress is in contrast to previous studies which have demonstrated acute stress to increase *ad libitum* alcohol

consumption in heavy drinkers (McGrath et al., 2016) and alcohol dependent individuals (Thomas et al., 2011). This finding also contrasts those studies which demonstrated social drinkers will readily consume more alcohol following stress (de Wit et al., 2003; Magrys & Olmstead, 2015) and longitudinal evidence that suggests a causal relationship between stress and drinking (Boden et al., 2014; Russell et al., 1999). Indeed, the lack of association between 'reactive' inhibitory control and *ad libitum* alcohol consumption in both sessions is in contrast to previous findings (Field & Jones, 2017; Jones, Field, et al., 2013; Weafer & Fillmore, 2008), however McGrath et al (McGrath et al., 2016) also failed to demonstrate this following acute stress. Contrastingly, there was an association between poorer proactive stopping and increased alcohol consumption following acute stress. This offers some support to researchers (e.g. (Aron, 2011)) who have argued proactive control may be a useful explanation of substance use behaviour. However, multiple regression analyses (see supplementary materials) showed that proactive stopping did not predict alcohol consumption when entered into a model with reactive stopping and proactive slowing, re-emphasising that this relationship is moderate and not robust.

With regards to the neurophysiological results, there was no effect of acute stress on P300 or N200 responses. This is in contrast to Dierolf et al (Dierolf et al., 2017), who also failed to find behavioural differences, but reported N200 and P300 differences following stress (compared to control) in healthy males. Indeed, Ceballos et al (Ceballos et al., 2012) also reported that stress increased N200 amplitudes in social drinkers, although they too failed to find an effect of stress on P300 amplitudes. Alcohol-cue exposure also had no effect on N200 responses, contrasting Watson et al (Watson et al., 2016), who demonstrated decreased N200 components following exposure to alcohol-cues (compared to neutral-cues). Contrastingly, P300 responses were significantly higher for alcohol-related images compared to neutral-related images. As the sample consisted of heavy drinkers, this finding is in partial support of research (e.g. (Herrmann et al., 2001; Littel et al., 2012; Namkoong, Lee, Lee, Lee, & An, 2004)) reporting that P300 amplitudes are increased in response to alcohol-related cues (compared to neutral-related cues) in substance users compared to controls. This may represent increased salience to alcohol-related cues in the current sample. Bartholow et al (Bartholow et al., 2007) also reported this in those with a LS to alcohol (but not HS individuals), however we failed to demonstrate a relationship between alcohol sensitivity and P300 responses. Indeed, alcohol sensitivity was not associated with alcohol use or proactive control in contrast to previous findings (Bailey & Bartholow, 2016; Fleming & Bartholow, 2014). Furthermore, neither P300 nor N200 responses in either session were associated with

ad libitum alcohol consumption contrasting Jones et al (Jones, Field, et al., 2013), and Bartholow et al (Bartholow et al., 2007) who reported a relationship with self-reported alcohol consumption.

Lastly, acute stress had no effect on WMC. This is contradictory to previous findings (e.g. (Luethi et al., 2008; Oei et al., 2006; Schoofs et al., 2008)), although there are other contrasting results (e.g. (Lukasik, Waris, Soveri, Lehtonen, & Laine, 2019)). Poorer WMC was however associated with worse proactive inhibition, which is supportive of previous findings (Richmond et al., 2015; Wiemers & Redick, 2018), and may suggest that individuals with a high WMC are better at goal maintenance compared to those with a low-WMC (Richmond et al., 2015). However, this was only the case following acute stress (i.e. not during the control session) and the clinical application of this finding is limited as WMC was not associated with alcohol use, in contrast to past research (Mahedy et al., 2018; Peeters et al., 2015; Thush et al., 2008). Thus, taking these findings and those regarding alcohol sensitivity into account, we found limited evidence of WMC or AS as mechanisms underlying effective proactive control.

However, it should be noted that these findings offer support for models which suggest inhibitory control is a multi-component processes (e.g. (Verbruggen, McLaren, et al., 2014)) which is comprised of both proactive and reactive control. In support of previous findings (Verbruggen et al., 2005; Verbruggen et al., 2006; Verbruggen, Stevens, et al., 2014), participants slowed down their responses as stop-signal probability increased. Furthermore, we were also able to isolate proactive stopping through the inclusion of a cue indicating stop-signal probability based on past research (Brevers et al., 2017; Verbruggen & Logan, 2009b). Indeed, participants made more inhibition errors for no-cue trials compared to cued trials suggesting they prepared themselves to detect stop-signals through proactive adjustments of their behaviour, when a stop-signal cue was presented, in line with previous studies (Elchlepp et al., 2016; Verbruggen & Logan, 2009b; Zandbelt et al., 2011).This likely explains the finding that SSRTs were faster to no-cue trials (compared to cued trials) as participants slowed down their responses to cued trials.

Nevertheless, these findings should be interpreted in light of limitations. Although the stress-manipulation was successful, nineteen participants reported being aware that the presentation task was designed to induce stress. Upon removal, there was no longer a main effect of image on proactive stopping and P300 responses. However, this may have been caused by a reduction in statistical power (see supplementary materials for further analyses). This level of awareness was likely the result of a within-subjects design, in which the stress

manipulation was the only change across the conditions. Furthermore, as McGrath et al (McGrath et al., 2016) note, this number may have been influenced by the requirement for participants to fill in a questionnaire assessing their state anxiety shortly before and after the presentation task. Certainly, the open question asking participants to guess the purpose of the study showed that only three were actually aware of the overall purpose of the study, and removal of these actually added a main effect of condition on SSRTs ($p=.046$, $\eta_p^2= .12$), suggesting that acute stress may indeed have an impact on reactive stopping.

Secondly, the sample consisted only of heavy drinkers. Future research would benefit from the inclusion of a control group of light drinkers or those who abstain from alcohol use to allow for comparison of impairments in inhibitory control across groups. This would be particularly useful as studies that have compared the effect of alcohol-cue exposure on inhibitory control in heavy drinkers vs. a control group of light drinkers have yielded contradictory results (e.g. (Czapla et al., 2016; Nederkoorn et al., 2009), and Sharma (Sharma, 2017) reported differences in the ability to implement proactive control in heavy vs. light drinkers. It would also be useful to examine the effect of low, moderate and high levels of stress on both reactive and proactive control. This could potentially explain the 'null' findings in the current study, and would help to confirm whether the effect of acute stress on inhibitory performance follows a U-shaped function (see (Henderson et al., 2012)). However, without a robust relationship between inhibitory processes and alcohol use, the clinical application of these findings would be limited.

In conclusion, the results demonstrated that acute stress had limited effects on reactive stopping, and no effect on proactive inhibitory processes or the neurological correlates of inhibitory control. Alcohol-cue exposure also had no effect on reactive stopping. However, alcohol-cue exposure did impair proactive stopping and increase P300 responses (compared to neutral-related cues). We also found limited evidence to suggest that working memory processes underlie proactive control. These results support that inhibitory control is a multi-component process. However, we only demonstrated limited support for models that suggest impairments in inhibitory control fluctuate in response to psychological processes and the environment. Indeed, there was also little evidence of a relationship between inhibitory control processes and *ad libitum* alcohol consumption.

Table 4: Descriptive statistics and Pearson's correlations for proactive and reactive inhibitory processes, P300 and N200 responses to alcohol-related cues, alcohol sensitivity, Working Memory Capacity and *ad libitum* alcohol consumption, for the stress condition.

	Mean (SD)	2	3	4	5	6	7	8
Reactive control	312.64 (66.63)	.21	.53**	-.29	-.24	-.04	.32	.20
Proactive slowing	141.60 (112.43)	-	-.38*	.16	-.13	.04	-.22	-.10
Proactive inhibition	9.53 (14.80)		-	-.22	.37*	-.19	.37*	.36*
P300	2.12 (1.55)			-	-.09	-.04	.11	.10
N200	0.08 (0.69)				-	-.32	-.01	.22
Alcohol sensitivity	0.02 (0.70)					-	.01	.01
Working Memory	8.19 (2.89)						-	.17
Alcohol consumption	48.57 (22.78)							-

*Reactive control = SSRTs (higher scores = worse reactive control). Proactive slowing = RT slowing in the stop-signal block compared to the no-signal block. Proactive inhibition = % of inhibition errors. P300/N200 = amplitudes of ERP responses to alcohol-related cues. Alcohol sensitivity = composite score of alcohol sensitivity. Working Memory = errors on SOPT. Alcohol consumption = beer consumed as a % of total fluid in the ad libitum taste test. *p<. 05, **p< .01*

Table 5: Descriptive statistics and Pearson's correlations for proactive and reactive inhibitory processes, P300 and N200 responses to alcohol-related cues, alcohol sensitivity, Working Memory Capacity and *ad libitum* alcohol consumption, for the control condition.

	Mean (SD)	2	3	4	5	6	7	8
Reactive control	296.18 (48.15)	.24	-.39*	-.22	.34	.07	-.17	-.13
Proactive slowing	160.02 (78.28)	-	-.44**	-.15	-.34	-.04	-.09	.08
Proactive inhibition	7.28 (6.12)		-	.11	-.00	-.23	.18	.10
P300	2.61 (1.83)			-	.16	.04	-.26	-.22
N200	0.15 (1.14)				-	.21	-.15	-.21
Alcohol sensitivity	0.02 (0.70)					-	-.09	-.03
Working Memory	8.22 (2.25)						-	.24
Alcohol consumption	47.32 (24.15)							-

*Reactive control = SSRTs (higher scores = worse reactive control). Proactive slowing = RT slowing in the stop-signal block compared to the no-signal block. Proactive inhibition = % of inhibition errors. P300/N200 = amplitudes of ERP responses to alcohol-related cues. Alcohol sensitivity = composite score of alcohol sensitivity. Working Memory = errors on SOPT. Alcohol consumption = beer consumed as a % of total fluid in the ad libitum taste test. *p<.05, p<.001*

6.6. Supplementary Information

6.6.1 Results

Craving (see table 1)

A 3 (subscale: mean scores on Inclined/Indulgent, Obsessed/Compelled, Resolved/Regulated) x 2 (condition: control, stress) x 2 (time: start of session, post-cognitive tasks) repeated measures ANOVA was conducted on scores on the AAAQ. This revealed main effects of scale ($F (2, 65) = 161.66$, $p<.001$, $\eta_p^2= .81$) and condition ($F (1, 39) = 7.04$, $p= .011$, $\eta_p^2= .15$) which showed that scores were higher overall in the stress session compared to the control session. However, there were no other significant main effects or interactions (ps> .05).

Table 1: Mean scores on the subscales of the AAAQ at the beginning of the sessions (Time 1) and post manipulation/computer tasks (values are mean, SD).

	Control Condition		Stress Condition	
	Time 1	Time 2	Time 1	Time 2
Inclined/Indulgent	4.43 (1.75)	4.68 (1.85)	4.77 (1.80)	4.88 (1.83)
Obsessed/Compelled	1.14 (1.23)	1.31 (1.43)	1.44 (1.36)	1.41 (1.51)
Resolved/Regulated	1.17 (1.17)	1.04 (1.06)	1.32 (1.42)	1.29 (1.37)

The associations between proactive and reactive control and ad libitum alcohol consumption.

Multiple regression analyses were conducted to investigate if proactive and reactive control predicted unique variance in alcohol consumption, separately for each session. Variance Inflation Factors (VIFs) ranged between 1.18 and 2.16 suggesting no issues with multi-collinearity. The full regression models did not predict significant variance in alcohol consumption (stress ($R^2 = .13$; $F (3, 34) = 1.68$, $p= .189$; control ($R^2 = .04$; $F (3, 34 = 0.47$, $p= .706$). Following acute stress, neither SSRTs ($\beta = -.03$, $p= .904$, 95% CI -.16 to .14), proactive slowing ($\beta = .06$, $p= .775$, 95% CI -.07 to .10) nor proactive stopping ($\beta = .39$, $p =.104$, 95% CI -.13 to 1.33) were predictive of *ad libitum* alcohol consumption. Furthermore, neither SSRTs ($\beta = -.12$, $p=.514$, 95 % CI -.25 to .13), proactive slowing ($\beta = .16$, $p= .390$,

95% CI -.07 to .17) or proactive stopping (β = .12, p= .550, 95% CI -1.12 to 2.06) were predictive of alcohol intake in the control session.

The associations between neurological responses to alcohol-cues and ad libitum alcohol consumption.

Multiple regression analyses were conducted to investigate if the magnitude of N200 and P300 responses to alcohol-cues predicted unique variance in alcohol consumption for each condition separately. VIFs ranged between 1.01 and 1.03 suggesting no issues with multi-collinearity. The full regression models did not predict a significant amount of variance in alcohol consumption in the stress session (R^2 = .06; F (2, 30) = 1.03, p= .370) or control session (R^2 = .08; F (2, 30) = 1.31, p= .284). Specifically in the stress session, neither P300 amplitudes (β= .13, p= .486, 95% CI -.35 to 7.22) nor N200 amplitudes (β= .23, p= .201, 95% CI -4.36 to 19.89) were predictive of significant variance in alcohol consumption. Similarly, neither P300 amplitudes (β= -.19, p= .294, 95% CI -7.29 to 2.29) nor N200 amplitudes (β= -.18, p= .308, 95% CI -11.60 to 3.78) in the control session were predictive of significant alcohol consumption.

Awareness of experimental aims

In this study we checked participants' awareness of our experimental aims. Three participants guessed the full aims (inferred from an open ended question). Removal of these did not significantly affect the results with regards to proactive stopping or slowing. However, the main effect of condition on reactive stopping was now significant (p=.046, η_p^2= .12). Nineteen participants also guessed the aim of the presentation task was to induce stress. There was no effect on the results regarding SSRTS or proactive slowing, however the main effect of image proactive stopping was removed. This was likely due to a reduction in statistical power. In terms of the neurophysiological results, removal of these participants removed the main effect of image on P300 responses which had demonstrated that mean amplitudes were significantly higher for alcohol-related images compared to neutral-related images and the condition * cue, image * electrode interactions. However, this was likely influenced by a reduction in power. Contrastingly, there was now an image * cue * electrode interaction which showed that P300 amplitudes were higher in the Cz electrode for alcohol-related images (compared to neutral-related) on no-cued trials. Removal of these participants had no effect on the N200 responses.

Furthermore, thirteen participants guessed the aim of the Stop-Signal task was to assess behavioural impulsivity (response inhibition). Upon removal, this removed the condition * cue interaction suggesting that acute stress no longer impaired reactive stopping to cued trials. Removal of these participants had no effect on proactive stopping. With regards to proactive slowing, removal of these participants added a condition * image interaction which showed that participants responded faster to alcohol-cues (compared to neutral cues) regardless of session and responded faster to neutral-cues in the control session (compared to the stress).

With regards to the neurophysiological results, removal of these only removed the condition * cue interaction on P300 amplitudes which had no significant post-hoc tests anyway. Removal of these also added an image * cue interaction on N200 amplitudes which was the result of significantly lower amplitudes for alcohol-related images compared to neutral-images for no-cued trials. Amplitude of N200 responses were also significantly higher for no-cued images (compared to cued) for neutral-related images. Lastly, eight participants guessed the aim of the taste test was to measure how much they drank. However, removal of these had no effect on the null finding with regards to beer consumption in the control vs. stress sessions.

6.7 Chapter Summary

This chapter contributed to the key aims of this thesis by demonstrating limited evidence that inhibitory processes fluctuate in response to psychological triggers. Contrastingly, alcohol-cue exposure did impair proactive stopping and increase P300 responses. This strengthens the suggestion that investigating only reactive stopping is of limited theoretical benefit. However, there was little evidence of a relationship between inhibitory processes (or neurophysiological responses) and alcohol consumption, or for the suggestion that Working Memory Capacity or alcohol sensitivity may underlie the effective use of proactive control. These findings are discussed in the following chapter, alongside the other findings reported in experimental chapters one to five.

Chapter 7

General Discussion

This thesis had two primary aims. The first aim was to isolate reactive control from proactive slowing in heavy drinkers, based on evidence from Verbruggen et al (Verbruggen, McLaren, et al., 2014), to confirm that that there is an *over-simplistic* conceptualisation of inhibitory control as a reactive stopping response in the addiction literature, with little acknowledgement of other inhibitory processes that may contribute to a better explanation of substance use behaviour (Aron, 2011; Brevers et al., 2017). The second aim was to investigate if these processes fluctuate *within* individuals in response to certain environmental and psychological triggers (alcohol intoxication, alcohol-cue exposure and exposure to acute stress), based on two theories (de Wit, 2009; Jones, Christiansen, et al., 2013), and whether these impairments predicted increased alcohol-seeking in non-dependent drinkers. Lastly, I also sought to investigate the potential mechanisms which may underlie the ability to implement proactive control effectively (alcohol sensitivity (AS) and Working Memory Capacity (WMC)). These research questions were important to provide knowledge on which specific inhibitory processes (if any) were impaired by psychological and environmental triggers, and which processes (if any) were related to increased alcohol consumption. This knowledge was required to update contemporary theories of addiction (e.g. (de Wit, 2009; Goldstein & Volkow, 2002; Jones, Christiansen, et al., 2013)), but also to identify if these processes could be targeted within addiction interventions. Therefore, throughout this thesis I recruited non-dependent heavy drinkers as this population is at risk for developing Alcohol Use Disorders. This chapter first summarises the main findings from each study. Following this, is a discussion of findings across studies in relation to contemporary models of addiction and past literature.

7.1 Summary of Main findings in each study

Study one aimed to isolate proactive slowing and reactive control in heavy drinkers, and investigate whether individual differences in these processes were associated with individual differences in self-reported alcohol consumption. The results demonstrated that reactive control and proactive slowing could be isolated in heavy drinkers. Specifically, heavy drinkers employed proactive slowing strategies as the probability of an inhibitory response

was increased, in both the Stop-Signal tasks and the AX-Continuous Performance Test, suggesting that inhibitory control is a multi-component process comprised of both reactive and proactive control. Despite this, individual differences in reactive control and proactive slowing were unrelated to individual differences self-reported alcohol use. Therefore, I failed to support my primary hypothesis. However, this study was important in allowing me to identify a task I could use moving forward with the research in this thesis. I conducted a split-third reliability analysis on all tasks which demonstrated that they all surpassed the .70 cut off for good internal reliability (Kline, 1999). I therefore chose the task that I thought would be most practical to incorporate alcohol-cues. I also conducted a Principal Component Analysis to investigate if the measures of proactive and reactive control loaded onto the same factors across tasks. However, these measures loaded onto one factor per task, but this was likely influenced by the methodological differences between tasks.

Following on from this, studies two and three aimed to investigate if alcohol-cue exposure (study two) and alcohol intoxication (study three) impaired proactive slowing and reactive control. I also modified a Stop-Signal task from study one to allow measurement of signal detection (i.e. detection of a stop-signal) to enable investigation into whether this process was also impaired by alcohol-cue exposure and alcohol intoxication. Lastly, as alcohol-cue exposure and alcohol intoxication have been shown to increase alcohol-seeking in non-dependent drinkers (Christiansen et al., 2013; de Wit & Chutuape, 1993; Fatseas et al., 2015; MacKillop & Lisman, 2007), I also aimed to investigate whether alcohol-cue exposure and alcohol intoxication increased *ad libitum* alcohol consumption, and whether impairments in inhibitory processes mediated this relationship. The results showed that alcohol-cue exposure did not significantly impair proactive slowing or signal detection. Indeed, following alcohol-cue exposure, SSRTs were unexpectedly quicker (indicating better reactive control), compared to neutral-cue exposure. Although this effect was abolished when I only compared blocks in the task in which the stop-signals were presented centrally (this methodology is more comparable to past literature (e.g. (Field & Jones, 2017; Kreusch, Vilenne, & Quertemont, 2013; Petit et al., 2012)). Contrastingly, this study did demonstrate that alcohol-cue exposure significantly increased a*d libitum* alcohol consumption and had a weak effect on craving (supporting e.g. (Christiansen et al., 2017; Fatseas et al., 2015; Jones, Rose, et al., 2013)). However, despite the increase in alcohol-seeking, there was no association between inhibitory processes and increased *ad libitum* alcohol consumption. Therefore, I found no support for the prediction that impairments in these processes would mediate the relationship between alcohol-cue exposure and increased alcohol-seeking.

Similarly, the results of study three demonstrated that alcohol intoxication did not impair proactive slowing nor signal detection. However, alcohol intoxication did impair reactive control (demonstrated through slower SSRTs) compared to the placebo-alcohol supporting past research (e.g. (Fillmore et al., 2009; Marczinski et al., 2005; Weafer & Fillmore, 2008)), but not compared to the control beverage. This suggests that the impairing effect of alcohol intoxication on reactive control is limited to the pharmacological effects. Indeed, reactive control was unexpectedly better following the placebo-alcohol beverage compared to the control, suggesting reactive stopping was not impaired by the anticipated effects of alcohol. In contrast, alcohol intoxication significantly increased *ad libitum* alcohol consumption compared to the placebo-alcohol and control (supporting (de Wit & Chutuape, 1993; Fernie et al., 2012; Rose & Grunsell, 2008)), but there was no difference following the placebo and control. This suggests that alcohol-seeking was also not influenced by the anticipated effects of alcohol, although these results may have been influenced by a long interval between the intake of the placebo beverage and the taste test (Christiansen et al., 2013). Lastly, I hypothesised that impairments in inhibitory processes following alcohol intoxication (compared to placebo-alcohol and control) would predict unique variance in alcohol consumption. However, no evidence for this was found nor for the prediction that impairments in these processes would mediate the relationship between alcohol priming and increased alcohol-seeking.

In two online studies (study four and five) I then aimed to clarify the role of reactive control and proactive control in heavy drinkers *outside* of the laboratory. I also examined potential mechanisms that could underlie the preparation of responses (WMC (study four and five) and AS (study five)). The results of study four demonstrated that poorer WMC (and increased alcohol craving) was associated with increased overall alcohol use (supporting (Bechara & Martin, 2004; Mahedy et al., 2018; Noël et al., 2001)). However, there were no associations between individual differences in proactive slowing or reactive control with individual differences in alcohol use. Furthermore, individual differences in proactive slowing were also unrelated to individual differences in WMC. Therefore, the assumptions required to examine mediation were not met. This hypothesis was also labelled as exploratory (and therefore not pre-registered), hence this analysis was not reported.

Similarly, the results of study five showed no associations between individual differences in reactive control or proactive slowing and overall alcohol use. Furthermore, there were no associations between individual differences in alcohol sensitivity and alcohol use or proactive slowing. Despite this, poorer WMC was associated with poorer proactive

slowing in support of my prediction and past literature (e.g. (Redick & Engle, 2011; Richmond et al., 2015; Wiemers & Redick, 2018)), but due to no association between individual differences in WMC and overall alcohol use, I did not meet the assumptions to investigate if WMC mediated the relationship between proactive slowing and alcohol use. Since this hypothesis (and the hypothesis regarding the mediating effect of AS) was labelled as exploratory (and not pre-registered), these analyses were not reported.

Lastly, study six aimed to investigate another factor (acute stress) which is thought to impair inhibitory control (Jones, Christiansen, et al., 2013). In particular, there is limited evidence regarding this effect and the studies which have been conducted have provided contradictory evidence. Additionally, this study aimed to provide neurophysiological evidence (rather than just behavioural evidence) to provide a more sensitive investigation of short-term fluctuations of inhibitory control, and whether these are related to increased alcohol-seeking. Lastly, I sought to investigate the potential mechanisms (WMC, AS) which could explain these relationships in a laboratory environment.

The results showed that there was no effect of acute stress on proactive processes or the neurological correlates of inhibitory control. Indeed, acute stress only impaired reactive stopping to cued stop-signal trials. Furthermore, alcohol-cue exposure had no effect on reactive stopping or proactive slowing. However, alcohol-cue exposure was found to impair proactive stopping (the proportion of inhibition errors) and increased P300 responses, compared to neutral-cue exposure. Despite this, acute stress did not significantly increase alcohol-seeking and I found limited evidence for the associations between inhibitory processes (including the neurological components) and *ad libitum* alcohol consumption. Lastly, neither WMC nor AS were associated with *ad libitum* alcohol consumption, proactive slowing or P300 responses. Indeed, only poorer WMC was moderately associated with poorer proactive inhibition following acute stress.

7.2 *Over-simplification* of inhibitory control

Taken together, findings from studies one to six provided support for Verbruggen et al's (Verbruggen, McLaren, et al., 2014) model. I was able to consistently isolate proactive slowing and reactive control in heavy drinkers, and these samples displayed proactive slowing as the requirement for response inhibition increased in all Stop-Signal tasks (studies one to six) and an AX-Continuous Performance Task (study one). This was important as it

has been suggested that proactive control may provide a more appropriate explanation of substance use behaviour (Aron, 2011).

The isolation of proactive control in heavy drinkers supports research which has demonstrated that participants slow down their responses as stop-signal probability increases (Verbruggen et al., 2005; Verbruggen et al., 2006; Verbruggen, Stevens, et al., 2014). Furthermore, in study six I also isolated proactive stopping by incorporating a stop-signal cue to indicate stop-signal probability, based on previous research (e.g. (Brevers et al., 2017; Verbruggen & Logan, 2009b)). The findings of study six showed that heavy drinkers made more inhibition errors for trials with no stop-signal cue compared to trials with a stop-signal cue. This suggests the participants prepared themselves to detect a stop-signal when a stop-signal cue was presented and supports previous findings (Elchlepp et al., 2016; Verbruggen & Logan, 2009b; Zandbelt et al., 2011) that suggest we can proactively adjust our behaviour. As such, these results also demonstrated that SSRTs were faster to no-cue trials (compared to cued trials). It is likely this finding can be explained by participants proactively adjusting their behaviour (and slowing down), suggesting that proactive control does have downstream effects on SSRTs, and it is therefore important to recognise proactive processes to provide a full model of inhibitory control (Verbruggen, McLaren, et al., 2014).

Additionally, in study two and three I also isolated signal-detection in modified Stop-Signal tasks. This is an important process as if the stop-signal is not detected rapidly enough or detected at all, response inhibition will not be engaged or successful (Verbruggen, McLaren, et al., 2014). Furthermore, research has suggested that signal detection could be particularly key to explaining hazardous drug and alcohol use (Brevers et al., 2017), due to a difficulty in detecting inhibitory signals in typically 'noisy' surroundings in the real-world (e.g. in a busy pub or bar) (Verbruggen, Stevens, et al., 2014). Indeed, stopping times in both studies were slower when stop-signals were presented in the periphery of the computer screen compared to centrally. Exploratory analyses also revealed that participants in both studies made more errors on stop-signal trials when the stop-signals were presented in the periphery, compared to centrally. These results supports the notion that reactive stopping involves multiple processes that allow an individual to stop successfully, rather than simply the duration of the single stopping process (Verbruggen, McLaren, et al., 2014). To be specific, as well as a final motor-related process (the 'reactive' act of inhibiting or not), reactive stopping is also influenced by how quickly a stop-signal is detected. Despite this, group differences in stopping performance are generally attributed to the inhibition of motor responses and the influence of signal detection is regularly overlooked (Verbruggen,

McLaren, et al., 2014). Therefore, researchers should attempt to acknowledge this process when investigating inhibitory processes.

To summarise, heavy drinkers employed proactive strategies as the probability for the requirement of response inhibition increased. These samples were also faster at detecting stop-signals presented in the centre of the screen compared to when they were presented in the periphery. This suggests that a focus only on reactive stopping is *over-simplistic,* and moving forward researchers should acknowledge and measure other inhibitory processes in the addiction literature, otherwise they risk providing an incomplete model of inhibitory control (Verbruggen, McLaren, et al., 2014; Verbruggen, Stevens, et al., 2014) in substance use behaviour. Indeed, there are a lot of inconsistencies in the literature (e.g. (Fernie et al., 2010; Nederkoorn et al., 2009; Smith & Mattick, 2018)), which may be the result of 'invisible' factors (such as preparation and learning).

7.3 Inhibitory control as a state variable

Despite the above findings, the research in this thesis only provided limited support for theoretical models which suggest that inhibitory control is a state variable that fluctuates in response to psychological processes and environmental triggers (de Wit, 2009; Jones, Christiansen, et al., 2013). Without solid evidence for state fluctuations in inhibitory processes, it is hard to argue that inhibitory control deficits underlie a 'loss of control' over drinking. Furthermore, throughout this thesis, I have argued that that these theories based their assumptions on an *over-simplistic* conceptualisation of inhibitory control. However, these studies failed to find robust evidence of alcohol-cue exposure, alcohol intoxication or acute stress leading to short-term fluctuations in proactive inhibitory processes *within* individuals. The findings with regards to this are further discussed below.

7.3.1 Alcohol intoxication

With regards to the effect of alcohol priming, I did find some support for the suggestion that alcohol intoxication leads to state fluctuations in response inhibition in study three. Certainly, acute alcohol intoxication was found to impair reactive inhibitory control compared to a placebo-alcohol dose, which offers support to past research (e.g. (Fillmore et al., 2009; Marczinski et al., 2005; Weafer & Fillmore, 2008)). However, the addition of a control group revealed that the effect of alcohol intoxication on SSRTs is limited. Specifically, there was no

evidence of an impairing effect of alcohol compared to the control when analysing both peripheral and central stop-signal blocks, and only weak evidence when comparing central blocks only. This suggests that the impairing effect is limited and is contradictory of Christiansen et al (Christiansen et al., 2013) who demonstrated that an alcoholic prime impaired executive functioning compared to both a placebo-alcohol and control beverage. Indeed, reactive control was also better following the placebo-alcohol beverage compared to the control, suggesting that the anticipated effects of alcohol had no impairing effects. This is in contrast to past research (Christiansen et al., 2016), which demonstrated a placebo-alcohol impaired inhibitory control compared to a control, and Chrisitiansen et al (Christiansen et al., 2013) who showed no difference in executive functioning following a placebo-alcohol and control prime. Consequently, these findings only offer limited support to theories which posit inhibition as a state variable (de Wit, 2009; Jones, Christiansen, et al., 2013).

Additionally, alcohol intoxication did not impair detection of stop-signals, nor did a placebo-alcohol prime. This is in contrast to research that suggests alcohol intoxication impairs selective attention (Plawecki et al., 2018; Roberts et al., 2014), and therefore may increase the difficulty of detecting inhibitory signals in typically 'noisy' surroundings in the real-world (e.g. in a busy pub or bar) (Verbruggen, Stevens, et al., 2014). Lastly, I also found no evidence that the pharmacological or anticipated effects of alcohol impaired proactive slowing. It should be noted that there is very little literature to compare these findings to, although our findings were supportive of Campbell et al (Campbell et al., 2017) who also found that alcohol intoxication did not significantly impair proactive control. However, due to the paucity of literature it is plausible that an effect may exist particularly in other samples, such as those with an Alcohol Use Disorder. Nevertheless, I only found limited support for the argument that inhibitory control is a state variable, which fluctuates in response to alcohol intoxication.

7.3.2 Acute stress

Furthermore, I found limited effects of acute stress (compared to a control) on reactive stopping in study six. This contrasts previous literature (e.g. (Roos et al., 2017; Scholz et al., 2009; Starcke et al., 2016)) that has demonstrated short-term deficits in inhibitory control following exposure to acute stress, and models which argue inhibitory control fluctuates in response to psychological processes (de Wit, 2009; Jones, Christiansen, et al., 2013). These findings also contrast research that has demonstrated enhanced performance on inhibitory

tasks following acute stress (Constantinou et al., 2010; Schwabe et al., 2013). However, McGrath et al (McGrath et al., 2016) also reported 'null findings' in a similar sample. Certainly, the condition * cue interaction did demonstrate that stress impaired reactive stopping to cued trials (compared to control), but we hypothesised that the impairing effect of stress would be in response to alcohol-related cues only. Thus, our findings also contradict research which has demonstrated that acute stress increases attentional biases towards alcohol-related cues (Field & Powell, 2007; Field & Quigley, 2009), and impairs 'reactive' control following exposure to alcohol-related cues (Zack et al., 2011). However, the supplementary finding that removal of participants who were aware of the overall purpose of the study, added a main effect of condition on reactive stopping may suggest this effect warrants further investigation. Furthermore, I found no effect of acute stress on proactive slowing or proactive stopping. This also contradicts the concept that inhibitory control is a state variable that fluctuates *within* individuals in response to acute stress. However, to my knowledge there is a lack of research to compare these findings to, thus it is possible that an effect of acute stress on proactive processes does exist, and it is only with further research could this be revealed.

Lastly, with regards to neurophysiological responses, I found no effect of acute stress on P300 or N200 responses (i.e. the ERPS associated with aspects of inhibitory control (Enriquez-Geppert et al., 2010; Huster et al., 2013; Liu et al., 2015)). This finding offers some support to Ceballos et al (Ceballos et al., 2012) who also failed to find an effect of stress on P300 amplitudes. However, they did find that stress increased N200 amplitudes in social drinkers. Furthermore, the findings also contrast Dierolf et al (Dierolf et al., 2017), who although failed to find behavioural differences, reported increased P300 difference waves and decreased N200 difference waves following acute stress (compared to control) in healthy males. Taking these findings together, I provided limited behavioural and neurophysiological support for the suggestion that acute stress impairs reactive or proactive inhibitory control processes.

7.3.3 Alcohol-cue exposure

Importantly, I failed to replicate findings that support these models (de Wit, 2009; Jones, Christiansen, et al., 2013) to show alcohol-cue exposure leads to short-term impairments in 'reactive' inhibitory control in studies two and six. Indeed, reactive control was unexpectedly better following alcohol-cue exposure (study two) and there was no difference in reactive

stopping to alcohol-cues (compared to neutral-cues) in study six. Specifically in study two, this finding was when all blocks of the Stop-Signal task were included in the analyses (i.e. central and peripheral stop-signal blocks). When the analysis was conducted with only central stop-signal blocks, there was no difference in SSRTs following alcohol-cue exposure and neutral-cue exposure. Nevertheless, these findings are in contrast to previous research (Field & Jones, 2017; Kreusch, Vilenne, & Quertemont, 2013; Monk et al., 2016; Muraven & Shmueli, 2006; Petit et al., 2012; Weafer & Fillmore, 2012) that has demonstrated alcohol-cue exposure impairs 'reactive' inhibitory control in non-dependent drinkers. However, there is other evidence which has also failed to support this in non-dependent drinkers (Jones, Rose, et al., 2013; Nederkoorn et al., 2009) and male dependent drinkers (Mainz et al., 2012). Indeed, although the effect of alcohol-cue exposure on inhibitory control was found to be robust in a recent meta-analyses (Jones, Robinson, et al., 2018), the effect was suggested to be small (Standardised mean difference = -0.21, 95% CI = −0.32, −0.11). Nevertheless, our findings do not support the notion that alcohol-cue exposure impairs 'reactive' inhibitory control.

Furthermore, alcohol-cue exposure did not impair signal detection in study two. This contradicts research that suggests alcohol-cues may guide the selective attention of heavy drinkers (Townshend & Duka, 2001) and therefore prevent individuals detecting inhibitory signals in the environment. There was also no effect of alcohol-cue exposure on proactive slowing in study two or study six. Taken together, these findings fail to support the notion that impairments in inhibitory control processes fluctuate in response to the environment. However, I did find that alcohol-cue exposure impaired proactive stopping (the proportion of inhibition errors) compared to neutral-cue exposure in study six. Although there is a paucity of literature to compare this to, this finding could be argued to support Sharma (Sharma, 2017) who also demonstrated heavy drinkers having difficulty utilising proactive control in the presence of alcohol-related cues (compared to neutral cues), in a modified Stroop task. Indeed, Sharma inferred that heavy drinkers were relying on reactive control as a late correction mechanism to inhibit their responses. This finding therefore offers some support to the suggestion that inhibitory control is a state variable that fluctuates in response to alcohol-cue exposure

With regards to the neurophysiological responses, P300 responses to alcohol-cues were also found to be significantly increased (compared to neutral-cues) in study six. This finding supports previous research (e.g. (Herrmann et al., 2001; Littel et al., 2012; Namkoong et al., 2004)) that has also revealed increased P300 responses to alcohol-cues (compared to

neutral-cues) in substance users (compared to controls). Furthermore, this finding offers support to Bartholow et al (Bartholow et al., 2007) who also reported that P300 responses to alcohol-cues (compared to neutral-cues) were increased in those with a LS to alcohol (but not those with a HS to alcohol). However I failed to demonstrate a relationship between alcohol sensitivity and P300 responses. Furthermore, although past research has suggested decreased P300 responses during inhibition is a marker for risk of alcoholism (Hesselbrock et al., 2001; Kamarajan et al., 2005), the findings in this thesis suggest that P300 responses may also be related to cue-reactivity or salience to alcohol-related cues. However, alcohol-cue exposure had no effect on N200 responses in this study. This contrasts previous research that has demonstrated decreased N200 components following exposure to alcohol-cues (compared to neutral-cues) in non-dependent drinkers (Watson et al., 2016). Furthermore, although the functional specificity of the N200 component still has a degree of uncertainty (Dimoska et al., 2006), it could be argued that this refutes claims that N200 responses are related to response conflict (rather than response inhibition per se) (Donkers & van Boxtel, 2004; Enriquez-Geppert et al., 2010; Kok et al., 2004; Yeung et al., 2004), as it would be expected that if alcohol-cues are more salient than neutral-cues to heavy drinkers, they would experience a degree of response conflict which would be reflected in differences in N200 responses. To summarise, I failed to find that alcohol-cue exposure impairs reactive inhibitory control nor proactive slowing. However, alcohol-cue exposure was found to impair proactive stopping and increase P300 responses. Thus, I provided mixed support for inhibitory control as a state variable in response to alcohol-cue exposure.

7.4 Potential mechanisms

This thesis also investigated the potential mechanisms that may underlie effective response inhibition. However, I found very little support for the mechanisms explored. The results of study four demonstrated that poorer WMC (and increased alcohol craving) was associated with increased overall alcohol use. This supports evidence that has demonstrated that both heavy and dependent substance users display deficits in tasks that measure WMC (e.g. (Bechara & Martin, 2004; Mahedy et al., 2018; Noël et al., 2001)). However, there was no association between individual differences in WMC and overall alcohol use in the presence of alcohol-related cues in study five suggesting this relationship is not robust. In study six, I also failed to find an effect of acute stress on WMC in contrast to previous research (e.g.

(Luethi et al., 2008; Oei et al., 2006; Schoofs et al., 2008)), although there are other contrasting results in the literature (e.g. (Lukasik et al., 2019)).

Despite this, I did demonstrate that poorer WMC was associated with poorer proactive slowing in study five and worse proactive inhibition in study six. These findings support past literature that has demonstrated WMC predicts performance on inhibitory control tasks and that individuals with a lower-WMC tend to be less proactive than those with a higher-WMC (Redick & Engle, 2011; Richmond et al., 2015; Wiemers & Redick, 2018). Certainly, this relationship could have useful real-world implications. It is possible that high-WMC individuals have an increased ability to initiate and maintain goals (in this case response selection) to guide their behaviour, compared to low-WMC individuals who rely more on reactive control (Richmond et al., 2015). However, correlation analyses in studies four to six also demonstrated WMC was not associated with reactive control, nor P300 responses. Therefore, it is hard to suggest those with a low-WMC rely more on their reactive control. Additionally, the relationships between proactive inhibitory processes and WMC did not exist in the presence of neutral-related cues in study four and only existed following acute stress (i.e. not during the control session) in study six. Certainly, the clinical application of these findings are limited by a lack of robust relationship between WMC and alcohol use.

Furthermore, in contrast to previous research that has suggested alcohol sensitivity is a risk factor for alcohol misuse and dependence (Fleming & Bartholow, 2014; Schuckit & Smith, 2000), individual differences in alcohol sensitivity were unrelated to individual differences in alcohol use in study five and study six. In both studies, I also failed to find an association between individual differences in alcohol sensitivity and proactive inhibitory processes or P300 responses. This fails to support Bailey and Bartholow (Bailey & Bartholow, 2016), who suggested that those with a low sensitivity to alcohol may be unable to utilise proactive control efficiently in the presence of alcohol-related cues. This also fails to support ERP research that has demonstrated increased P300 amplitudes in individuals with a low sensitivity to alcohol, in response to alcohol-related cues (Bartholow et al., 2007; Bartholow et al., 2010). Consequently, I found limited evidence of WMC or AS as mechanisms underlying effective reactive or proactive control.

To summarise so far, the studies in this thesis have provided evidence that inhibitory control is a multi-component process, which is comprised of both reactive and proactive control. However, with the exception of an impairing effect of alcohol-cue exposure on proactive stopping in study six, I failed to find robust evidence that proactive inhibitory processes are impaired by alcohol-cue exposure, acute alcohol intoxication or acute stress.

Furthermore, there were only limited effects of alcohol intoxication and acute stress on reactive stopping, and no impairing effects of alcohol-cue exposure. In addition, there was no evidence that acute stress affected the neurophysiological responses associated with inhibitory control, although alcohol-cue exposure did increase P300 amplitudes (compared to neutral-cue exposure). Lastly, I have found little evidence that WMC or AS are mechanisms which underlie the effective use of proactive control, or mediate the relationships between inhibitory processes and alcohol use.

7.5 Relationship between inhibitory control processes and alcohol consumption

The results of this thesis also provide little evidence that individual differences in inhibitory processes are related to alcohol use. Specifically, the results of study two and three did demonstrate that alcohol-cue exposure and alcohol intoxication significantly increased *ad libitum* alcohol consumption and had a weak effect on craving. This is in line with other research that has revealed increased alcohol-seeking following alcohol-cue exposure (Christiansen et al., 2017; Fatseas et al., 2015; Jones, Rose, et al., 2013; Koordeman et al., 2011; MacKillop & Lisman, 2007) and alcohol intoxication in both heavy drinkers and alcohol dependent individuals (de Wit & Chutuape, 1993; Fernie et al., 2012; Rose & Grunsell, 2008). However, there was no significant difference in *ad libitum* alcohol consumption following the placebo-alcohol compared to the control in study three. This does support previous research (Christiansen et al., 2013) suggesting that it is only alcohol's pharmacological effects (and not the anticipated effects) which are key to the alcohol priming effect. However, other studies have demonstrated that a placebo-alcohol beverage increases subsequent subjective (e.g. self-reported craving) and/or objective (e.g. bogus taste test) measures of alcohol seeking (Christiansen et al., 2016; Christiansen et al., 2017). These past findings suggest that increases in craving and alcohol-seeking following an alcoholic priming drink are at least partially the result of the anticipated effects of alcohol and not solely the pharmacological effects (Christiansen et al., 2017).

However, although alcohol-cue exposure and alcohol intoxication increased *ad libitum* alcohol consumption, there were no robust effects on craving. This is in contrast to previous studies (e.g. (Christiansen et al., 2013; Fatseas et al., 2015; Field & Jones, 2017; Rose et al., 2013)), but does suggest that alcohol-seeking can increase without an accompanied increase in self-reported craving, a result which has also been reported in

previous literature (e.g. (Wiers et al., 2010) see also (Tiffany, 1990; Wiers et al., 2007)). Nevertheless, in both of these studies individual differences in inhibitory processes were unrelated related to *ad libitum* alcohol consumption. This contrasts previous studies (Field & Jones, 2017; Jones, Field, et al., 2013; Weafer & Fillmore, 2008). Specifically, we failed to replicate studies that have found impairments in inhibitory control partially mediated the relationship between alcohol-cue exposure and increased alcohol-seeking (Field & Jones, 2017), or moderated the relationship between alcohol-cue exposure and increased craving in heavy drinkers (Papachristou, Nederkoorn, Havermans, et al., 2012). However, Jones et al (Jones, Rose, et al., 2013) also failed to demonstrate that individual differences in inhibitory control were associated with alcohol-seeking following alcohol-cue exposure. Nevertheless, we also failed to support studies that have demonstrated this relationship following alcohol intoxication. For example, Weafer and Fillmore (Weafer & Fillmore, 2008) demonstrated that individual differences in the degree of impairment in inhibitory control from alcohol intoxication were positively associated with *ad-libitum* alcohol consumption. However, in this study the alcohol prime was not consumed in the same testing as session as the measure of alcohol-seeking and therefore this does not explain whether alcohol-induced impairments in inhibition mediated the alcohol priming effect (Knibb et al., 2018). Indeed, the results of this thesis suggest it is unlikely that increased alcohol-seeking following alcohol-cue exposure and intoxication is the result of impairments in inhibitory processes.

Furthermore in study six, acute stress did not reliably increase self-reported craving or *ad libitum* alcohol-seeking (compared to a control). This is in contrast to previous studies which have demonstrated that acute stress increases craving (Field & Powell, 2007) and alcohol consumption in heavy drinkers (McGrath et al., 2016) and alcohol dependent individuals (Thomas et al., 2011). This finding also contradicts studies that have demonstrated that social drinkers readily consume more alcohol following stress (de Wit et al., 2003; Magrys & Olmstead, 2015), and longitudinal evidence, which implies a causal relationship between stress and alcohol use (Boden et al., 2014; Russell et al., 1999). However, the lack of association between individual differences in reactive control and increased alcohol-seeking following acute stress does offer support to some studies (McGrath et al., 2016). Indeed, there was also a relationship between poorer proactive stopping and increased alcohol-seeking following acute stress in this study. This finding does offer some support to researchers (e.g. (Aron, 2011)) who have argued proactive control may be a useful explanation of substance use behaviour. However, this correlation was only moderate and is limited due to the non-significant difference in alcohol-seeking following acute stress

compared to the control session, and the null finding with regards to the effect of stress on proactive stopping. Indeed, proactive stopping was not a significant predictor of *ad libitum* alcohol consumption when entered into a multiple regression model with SSRTs and proactive slowing. Notably, in this study neither P300 nor N200 responses following acute stress (and the control session) were associated with *ad libitum* alcohol consumption, in contrast to Jones et al (Jones, Field, et al., 2013), as well as Batholow et al (Bartholow et al., 2007) who demonstrated a relationship between P300 responses and self-reported alcohol use.

Lastly, we also failed to find support for the associations between individual differences in reactive control or proactive slowing and individual differences in self-reported alcohol use in studies one, four and five. Hence, we failed to find support for studies that have demonstrated a relationship between 'reactive' inhibitory control and alcohol use (Christiansen, Cole, Goudie, et al., 2012; Colder & O'Connor, 2002; Houston et al., 2014; Murphy & Garavan, 2011). However, there are other studies, which have also reported contradictory findings (e.g. (Bø & Landro, 2017; Fernie et al., 2010)) or demonstrated very little evidence of inhibitory control deficits in heavy drinkers (e.g. (Bednarski et al., 2012; Franken et al., 2017; Nederkoorn et al., 2009)). Importantly, these findings fail to support models of addiction that posit inhibitory control as a candidate mechanism for substance addiction (de Wit, 2009; Fillmore, 2003; Goldstein & Volkow, 2002). Taking this, and the limited evidence for fluctuating inhibitory processes into account, the theoretical implications of this thesis suggest that further clarification is necessary to understand the psychological mechanisms, which underlie a 'loss of control' over drinking. Further support for this suggestion has been found recently in a meta-analysis (Lui et al., 2019), which reported a null relationship between inhibitory control and the use of most substances. However, the authors did find that both sample (age, time in education) and task (the proportion of no-go trials in a Go/No-Go task) characteristics had a significant effect on inhibitory control performance. This led them to suggest that the relationship may only exist in extreme groups (i.e. addicted individuals), and certainly that both task and sample characteristics may play a role in detecting such a relationship. Thus, we cannot rule out the possibility that an association does exist in some groups, and it has just failed to be detected.

Indeed, Campbell et al (Campbell et al., 2017) found a smaller effect of alcohol intoxication on reactive inhibitory control than they predicted and therefore suggested the possibility of a lack of power and publication bias in the current literature. Furthermore, in their meta-analyses exploring the effect of alcohol-cues on inhibitory control, Jones et al

(Jones, Robinson, et al., 2018) report that the literature contains a number of poor quality studies with reporting biases and a lack of power. Based on the results of this thesis, it is certainly possible that the relationship between 'reactive' inhibitory control and alcohol use has been over-emphasised in the literature, particularly in non-dependent samples. In support of this, an updated meta-analyses by Smith et al (Smith & Mattick, 2018) failed to replicate their previous findings (Smith et al., 2014) of inhibitory deficits in non-dependent, heavy drinkers. Indeed, although it is possible that a relationship may still exist between proactive control and alcohol use due to a paucity of literature, this relationship would have to be considered in the broader context of an inconsistent or lack of association between reactive control and alcohol use in non-dependent drinkers.

Importantly, a key strength of this thesis is that the design, hypothesis and analysis strategies of studies two, three, five and six were all pre-registered on Open Science Framework. This should improve confidence in the findings due to the transparency of *a-priori* and exploratory hypotheses, and should also increase the ease of replication (Munafò et al., 2017). Certainly, Nosek et al (Nosek, Ebersole, DeHaven, & Mellor, 2018) argue that pre-registration is a useful solution to reducing biases in the literature. This is supported by findings which illustrate higher replicability in studies with *a-priori* hypotheses (Swaen, Teggeler, & van Amelsvoort, 2001), an increase in null findings (Kaplan & Irvin, 2015), and a reduction in effect sizes (Schäfer & Schwarz, 2019) following pre-registration. This suggests that various factors such as publication bias, researcher bias, as well as problematic research techniques may distort the true nature of true effects (Schäfer & Schwarz, 2019). Thus, it is only by continuing in the direction of well-powered and pre-registered studies can we begin to correct any biases in the literature and reveal the true relationship between inhibitory deficits and alcohol use in non-dependent samples. Indeed, it should be noted that the majority of power calculations in this thesis were based on medium effect sizes reported in previous studies. However, some research has since been published (e.g. (Jones, Robinson, et al., 2018)) which report smaller effect sizes. Therefore, the sample sizes recruited may have affected the results in this thesis. However, the consistent null findings reported throughout suggest that this is unlikely.

7.6 Clinical Implications

The results of this thesis suggest that the addiction field should acknowledge that inhibitory control is a multi-component process. Certainly, I demonstrated that alcohol-cue exposure

impaired proactive stopping in study six but this aside, I found little other evidence of state fluctuations in proactive inhibitory processes following alcohol intoxication, alcohol-cue exposure and acute stress. Thus, this offers little support to those who suggest proactive control may be a better explanation of impairments in inhibitory control in substance use behaviour compared to reactive stopping (e.g. (Aron, 2011)). Furthermore, although I found alcohol intoxication impaired SSRTs (albeit a limited effect), alcohol-cue exposure did not impair reactive stopping and acute stress (compared to control) only impaired reactive stopping to cued stop-signal trials. Indeed, the clinical significance of these limited findings are further restricted by the failure on the most part to demonstrate a relationship between inhibitory processes and alcohol use. Supporting this, Jones et al (Jones, Robinson, et al., 2018) also questioned the clinical significance of their finding that the effect of alcohol-cue exposure on reactive inhibitory control was robust, due to the small effect size and the questionable relationship between inhibitory control and substance use. As such, the only finding supportive of this relationship was in study six which demonstrated a moderate association between poorer proactive stopping and increased alcohol consumption following acute stress.

As a result of this, it is hard to argue for the development of addiction interventions targeting these effects to reduce drinking. Furthermore, those studies which have investigated the effect of training inhibitory control on alcohol use have yielded contradictory results. For example, we (Jones et al., 2019) recently carried out a study which supported a developing body of research (e.g. (Jones, McGrath, et al., 2018; Smith, Dash, Johnstone, Houben, & Field, 2017)) that suggests inhibitory control training (and also cognitive bias modification (Boffo et al., 2019)) is not effective in reducing alcohol use in heavy, non-dependent drinkers. The inhibitory training in this study also failed to improve both reactive stopping and proactive slowing in response to alcohol-related cues. Thus, without a robust relationship between inhibitory control and alcohol use and studies demonstrating successful training to reduce alcohol use, it is hard to argue for the clinical significance of the findings in this thesis. Consequently, it may be time future research look towards alternative processes to target for addiction interventions (Jones et al., 2019) or as stated, it is only with continuing in the direction of well-powered and pre-registered studies can we reduce bias in the literature and truly understand the relationship between inhibitory processes and alcohol use. Indeed, if a robust relationship was confirmed, Field et al (Field et al., 2019) argue that it is plausible to transfer results from experimental studies into behaviour change interventions outside of the laboratory, by following an Experimental Medicine Framework and considering

methodological problems (e.g. sample characteristics, demand effects) that may limit the transfer of interventions into real-world behaviour change.

7.7 Limitations

However, this thesis does have methodological limitations which may have impacted the results. Firstly, the sample mainly consisted of heavy drinking undergraduate students. I decided to recruit heavy drinkers as this sample are at risk for later development of substance dependence. However, I also aimed to recruit individuals who were motivated to cut down their drinking. Indeed, *'a motivation to reduce alcohol consumption'* was included in the inclusion criteria for each study. However, although motivations to cut-down drinking have been reported in young adults following alcohol-related accidents (Barnett, Goldstein, Murphy, Colby, & Monti, 2006; Barnett et al., 2002) or overdoses (Reis, Harned, & Riley, 2004), the majority of students remain heavy drinkers with little motivation to cut down (Field et al., 2019; Shealy, Murphy, Borsari, & Correia, 2007). This is suggested to be the case until they leave University and "mature" out of hazardous drinking for various reasons, such as increased emotional stability and self-control, which are related to a reduction in drinking for enhancement and coping motives (Littlefield, Sher, & Wood, 2010). Indeed, the measurement of motivation can also be challenging in students, as generally these samples are poor at problem recognition (Barnett et al., 2006), however I did attempt to measure "concerns about drinking" using the TRI (see Appendices 1.D). Nevertheless, it is plausible that the samples in this thesis may have had little motivation to inhibit their responses in the Stop-Signal tasks and restrict their alcohol intake in the *ad libitum* taste tests. This could have contributed to the lack of associations between inhibitory control and alcohol use in studies one to six.

In addition, as all participants were heavy drinkers, these studies did not include light drinkers or abstainers as controls. In particular, this would have been useful to compare the effects of alcohol-cue exposure between groups since the results showed that alcohol-cue exposure had differential effects on reactive and proactive stopping, in heavy drinkers. Indeed, studies that have compared the effect of alcohol-cue exposure on inhibitory control in heavy drinkers vs. a control group of light drinkers have yielded contradictory results (Czapla et al., 2016; Nederkoorn et al., 2009), and Sharma (Sharma, 2017) reported differences in the use of reactive and proactive control in heavy vs. light drinkers when completing a modified Stroop task, with preceding alcohol-related and neutral-related cues. This would also allow

further investigation into the effect of alcohol-cue exposure on P300 responses, as although our results suggested heavy drinkers showed increased salience to alcohol-cues (compared to neutral-cues), we were unable to compare this to light drinkers or abstainers. Lastly, since I failed to find main effects of acute stress on proactive or reactive inhibitory processes, it may be useful to compare these results to a group of light drinkers or abstainers. Certainly, previous research (e.g. (King, Munisamy, de Wit, & Lin, 2006)) has demonstrated differences in cortisol release following a heavy dose of alcohol in heavy compared to light drinkers.

Finally, throughout the research in this thesis, I used Stop-Signal tasks (Logan et al., 1984) to measure proactive and reactive inhibitory control. These are one of the most popular task paradigms used throughout the literature and I demonstrated good internal reliability of the task I took forward in study one. However, recent evidence has questioned the validity of these tasks in measuring executive functioning. In a sample of 463 undergraduate students, Von Gunten et al (Von Gunten, Bartholow, & Martins, 2019) reported a lack of association between inhibition (in a Stop-Signal task, Anti-Saccade task, Stroop task, Go/No-Go task and Simon task) and outcomes of self-regulation. This finding therefore questions the validity of inhibitory control measures. Additionally, I used these tasks to measure individual differences in proactive and reactive inhibitory control. However, Von Gunten et al suggest that there may not be enough between-subjects variance in these tasks to reliably rank inhibition scores. Furthermore, research (e.g. (Friedman & Miyake, 2004; Gärtner & Strobel, 2019)) has demonstrated low correlations between inhibitory control tasks. To give a specific example, one study (Gärtner & Strobel, 2019) demonstrated that correlation coefficients between six tasks (Stop-Signal, Word-Naming, Anti-Saccade, Stroop, Eriksen Flanker and Shape-Matching) were less than 0.3. Thus, this also challenges whether the commonly used inhibition tasks are reliable and valid measures of inhibition, which may have impacted the results.

7.8 Future research

As stated, this thesis aimed to investigate the relationship between inhibitory processes and alcohol use in those at risk for developing Alcohol Use Disorders. However, due to finding contradictory results, it would be useful to explore the relationship between reactive control, (and more so) proactive control and alcohol use in those with a past or current alcohol dependency. Certainly, Smith et al's original meta-analyses (Smith et al., 2014) demonstrated

that evidence of impairments in inhibitory control were more apparent in individuals who are alcohol dependent. Thus, this could provide a useful line of future research, and perhaps shed light on if a true relationship exists between inhibitory control and alcohol use in other samples. As mentioned, there is a paucity of research investigating proactive control and alcohol use, but Hu et al's (Hu et al., 2015) study, which reports differences in the proactive response adjustments (but not reactive control) in alcohol dependent patients vs. healthy controls, suggests this could warrant further investigation in these samples.

Furthermore, as I found no main effects of acute stress on reactive or proactive control (or the neurological correlates of response inhibition) in study six, it may be useful to investigate the effect of low, moderate and high acute stress on these processes to investigate whether there are differential effects of different levels of stress. This would contribute to the explanation of whether the effect of acute stress on inhibitory control follows a U-shaped function (see (Henderson et al., 2012)). Future research could also benefit from using more objective measures of stress, for example cortisol release (see (Hellhammer, Wüst, & Kudielka, 2009)) rather than self-report measures to eliminate any bias in the results. Lastly, it would be useful to develop these investigations outside of the laboratory. One possible technique could be to use an Ecological Momentary Assessment (EMA) method to investigate the effects of real-time alcohol intoxication, cue-exposure and acute stress on inhibitory control and the relationship with alcohol use. Indeed, Jones et al (Jones, Tiplady, et al., 2018) demonstrated that alcohol consumption increased as inhibitory control worsened throughout the day in their EMA study. Thus, it may be useful to also measure proactive slowing and signal detection in an EMA study of non-dependent drinkers. This would also allow comparisons between groups if heavy drinkers and light drinkers or abstainers were included. However as stated, without a robust relationship between inhibitory control and alcohol use, the clinical application of these findings would be limited. Certainly, any findings with regards to proactive control would have to be considered in the context of an inconsistent relationship between reactive inhibitory control and alcohol use.

7.9 Conclusion

In conclusion, the results of this thesis demonstrated that heavy drinkers are able to proactively adjust their behaviour as the requirement for response inhibition increases. This suggests that inhibitory control is a multi-component process which is comprised of both reactive and proactive control, and has been *over-simplified* in past literature. However, the

research in this thesis found only limited behavioural and neurophysiological evidence that impairments in inhibitory processes fluctuate *within* individuals in response to psychological and environmental triggers. In particular, there was a failure to replicate a seemingly robust effect of alcohol-cue exposure on impairments in reactive control, and only limited effects of acute stress and alcohol intoxication on reactive stopping. Contrastingly, there was evidence that alcohol-cue exposure increased P300 responses (compared to neutral-cue exposure). However, there was also very limited evidence for the potential mechanisms which may underlie these effects. Importantly, this thesis also found little evidence of a relationship between inhibitory process and alcohol consumption, suggesting this may have been over-emphasised in the literature. This therefore contradicts theories that posit inhibitory control as a key mechanism for substance addiction, and restricts the clinical significance of the current limited findings (and any future findings) which demonstrate inhibitory control is a state variable.

References

Abroms, B. D., & Fillmore, M. T. (2004). Alcohol-induced impairment of inhibitory mechanisms involved in visual search. *Experimental and Clinical Psychopharmacology, 12*(4), 243-250. doi:10.1037/1064-1297.12.4.243

Adams, S., Ataya, A. F., Attwood, A. S., & Munafo, M. R. (2013). Effects of alcohol on disinhibition towards alcohol-related cues. *Drug and Alcohol Dependence, 127*(1-3), 137-142. doi:10.1016/j.drugalcdep.2012.06.025

Alcohol units - A brief guide. (2008).

Arnsten, A. F. T. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience, 10*(6), 410-422. doi:10.1038/nrn2648

Aron, A. R. (2011). From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses. *Biological Psychiatry, 69*(12), e55-e68. doi:http://dx.doi.org/10.1016/j.biopsych.2010.07.024

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience, 6*(2), 115-116. doi:10.1038/nn1003

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. *Trends in Cognitive Sciences, 18*(4), 177-185. doi:10.1016/j.tics.2013.12.003

Babor, T. F., Higgins-Biddle, J., Saunders, J. B., & Monteiro, M. (2001). *The Alcohol Use Disorders Identification Test: Guideline for use in primary care*.

Baddeley, A. (1992). Working memory. *Science, 255*(5044), 556-559. doi:10.1126/science.1736359

Bailey, K., & Bartholow, B. D. (2016). Alcohol words elicit reactive cognitive control in low-sensitivity drinkers. *Psychophysiology, 53*(11), 1751-1759. doi:10.1111/psyp.12741

Baines, L., Field, M., Christiansen, P., & Jones, A. (2019a). The effect of alcohol cue exposure and acute intoxication on inhibitory control processes and ad libitum alcohol consumption. *Psychopharmacology, 236*(7), 2187-2199. doi:10.1007/s00213-019-05212-4

Baines, L., Field, M., Christiansen, P., & Jones, A. (2019b). Isolating Proactive Slowing from Reactive Inhibitory Control in Heavy Drinkers. *Substance Use & Misuse*. doi:10.1080/10826084.2019.1658783

Baines, L., Jones, A., & Christiansen, P. (2016). Hopelessness and alcohol use: The mediating role of drinking motives and outcome expectancies. *Addictive Behaviors Reports, 4*, 65-69. doi:http://dx.doi.org/10.1016/j.abrep.2016.11.001

Bakhshani, N.-M. (2014). Impulsivity: a predisposition toward risky behaviors. *International Journal of High Risk Behaviors & Addiction, 3*(2), e20428-e20428. doi:10.5812/ijhrba.20428

Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: behavioral and neural basis of response control. *Progress in Neurobiology, 108*, 44-79. doi:10.1016/j.pneurobio.2013.06.005

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychology Bulletin, 121*(1), 65-94. doi:10.1037/0033-2909.121.1.65

Barnett, N. P., Goldstein, A. L., Murphy, J. G., Colby, S. M., & Monti, P. M. (2006). "I'll never drink like that again": characteristics of alcohol-related incidents and predictors

of motivation to change in college students. *Journal of Studies on Alcohol and Drugs, 67*(5), 754-763. doi:10.15288/jsa.2006.67.754
Barnett, N. P., Lebeau-Craven, R., O'Leary, T. A., Colby, S. M., Wollard, R., Rohsenow, D. J., . . . Monti, P. M. (2002). Predictors of motivation to change after medical treatment for drinking-related events in adolescents. *Psychology of Addictive Behaviors, 16*(2), 106-112. doi:10.1037/0893-164X.16.2.106
Bartholow, B. D., Henry, E. A., & Lust, S. A. (2007). Effects of alcohol sensitivity on P3 event-related potential reactivity to alcohol cues. *Psychology of Addictive Behaviors, 21*(4), 555-563. doi:10.1037/0893-164X.21.4.555
Bartholow, B. D., Lust, S. A., & Tragesser, S. L. (2010). Specificity of P3 Event-Related Potential Reactivity to Alcohol Cues in Individuals Low in Alcohol Sensitivity. *Psychology of Addictive Behaviors, 24*(2), 220-228. doi:10.1037/a0017705
Bartholow, B. D., Pearson, M., Sher, K. J., Wieman, L. C., Fabiani, M., & Gratton, G. (2003). Effects of alcohol consumption and alcohol susceptibility on cognition: a psychophysiological examination. *Biological Psychology, 64*(1), 167-190. doi:https://doi.org/10.1016/S0301-0511(03)00108-X
Bartsch, A. J., Homola, G., Biller, A., Smith, S. M., Weijers, H.-G., Wiesbeck, G. A., . . . Bendszus, M. (2007). Manifestations of early brain recovery associated with abstinence from alcoholism. *Brain, 130*(1), 36-47. doi:10.1093/brain/awl303
Baumeister, R. F. (2014). Self-regulation, ego depletion, and inhibition. *Neuropsychologia, 65*, 313-319. doi:https://doi.org/10.1016/j.neuropsychologia.2014.08.012
Baumeister, R. F., Heatherton, T. F., & Tice, D. M. (1994). *Losing control: How and why people fail at self-regulation*. San Diego, CA, US: Academic Press.
Bechara, A., & Martin, E. M. (2004). Impaired decision making related to working memory deficits in individuals with substance addictions. *Neuropsychology, 18*(1), 152-162. doi:10.1037/0894-4105.18.1.152
Bednarski, S. R., Erdman, E., Luo, X., Zhang, S., Hu, S., & Li, C. S. (2012). Neural processes of an indirect analog of risk taking in young nondependent adult alcohol drinkers-an FMRI study of the stop signal task. *Alcoholism, Clinical and Experimental Research, 36*(5), 768-779. doi:10.1111/j.1530-0277.2011.01672.x
Bender, A. D., Filmer, H. L., Garner, K. G., Naughtin, C. K., & Dux, P. E. (2016). On the relationship between response selection and response inhibition: An individual differences approach. *Attention Perception Psychophysics, 78*(8), 2420-2432. doi:10.3758/s13414-016-1158-8
Berg, P., & Scherg, M. (1994). A multiple source approach to the correction of eye artifacts. *Electroencephalography and Clinical Neurophysiology, 90*(3), 229-241. doi:https://doi.org/10.1016/0013-4694(94)90094-9
Berger, I., Slobodin, O., & Cassuto, H. (2017). Usefulness and Validity of Continuous Performance Tests in the Diagnosis of Attention-Deficit Hyperactivity Disorder Children. *Archives of Clinical Neuropsychology, 32*(1), 81-93. doi:10.1093/arclin/acw101
Bickel, W. K., Jarmolowicz, D. P., Mueller, E. T., Gatchalian, K. M., & McClure, S. M. (2012). Are executive function and impulsivity antipodes? A conceptual reconstruction with special reference to addiction. *Psychopharmacology (Berl), 221*(3), 361-387. doi:10.1007/s00213-012-2689-x
Billieux, J., Gay, P., Rochat, L., Khazaal, Y., Zullino, D., & Van der Linden, M. (2010). Lack of inhibitory control predicts cigarette smoking dependence: evidence from a non-deprived sample of light to moderate smokers. *Drug and Alcohol Dependence, 112*(1-2), 164-167. doi:10.1016/j.drugalcdep.2010.06.006

Billieux, J., Lagrange, G., Van der Linden, M., Lancon, C., Adida, M., & Jeanningros, R. (2012). Investigation of impulsivity in a sample of treatment-seeking pathological gamblers: a multidimensional perspective. *Psychiatry Research, 198*(2), 291-296. doi:10.1016/j.psychres.2012.01.001

Bø, R., & Landro, N. I. (2017). Inhibitory control and response monitoring are not systematically related to weekly alcohol consumption in the general population. *Psychopharmacology (Berl), 234*(11), 1761-1768. doi:10.1007/s00213-017-4578-9

Boden, J. M., Fergusson, D. M., & Horwood, L. J. (2014). Associations between exposure to stressful life events and alcohol use disorder in a longitudinal birth cohort studied to age 30. *Drug and Alcohol Dependence, 142*, 154-160. doi:10.1016/j.drugalcdep.2014.06.010

Boden, J. M., Lee, J. O., Horwood, L. J., Grest, C. V., & McLeod, G. F. (2017). Modelling possible causality in the associations between unemployment, cannabis use, and alcohol misuse. *Social Science and Medicine, 175*, 127-134. doi:10.1016/j.socscimed.2017.01.001

Boffo, M., Zerhouni, O., Gronau, Q. F., van Beek, R. J. J., Nikolaou, K., Marsman, M., & Wiers, R. W. (2019). Cognitive Bias Modification for Behavior Change in Alcohol and Smoking Addiction: Bayesian Meta-Analysis of Individual Participant Data. *Neuropsychology Review, 29*(1), 52-78. doi:10.1007/s11065-018-9386-4

Bogg, T., & Finn, P. R. (2010). A self-regulatory model of behavioral disinhibition in late adolescence: integrating personality traits, externalizing psychopathology, and cognitive capacity. *Journal of Personality, 78*(2), 441-470. doi:10.1111/j.1467-6494.2010.00622.x

Boileau, I., Dagher, A., Leyton, M., Welfeld, K., Booij, L., Diksic, M., & Benkelfat, C. (2007). Conditioned Dopamine Release in Humans: A Positron Emission Tomography Study with Amphetamine. *The Journal of Neuroscience, 27*(15), 3998. doi:10.1523/JNEUROSCI.4370-06.2007

Braver, T. S. (2012). The variable nature of cognitive control: A dual mechanisms framework. *Trends in Cognitive Sciences, 16*(2), 106-113. doi:10.1016/j.tics.2011.12.010

Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L., & Snyder, A. (2001). Anterior Cingulate Cortex and Response Conflict: Effects of Frequency, Inhibition and Errors. *Cerebral Cortex, 11*(9), 825-836. doi:10.1093/cercor/11.9.825

Braver, T. S., Paxton, J. L., Locke, H. S., & Barch, D. M. (2009). Flexible neural mechanisms of cognitive control with human prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States of America, 106*, 7351-7356. doi:10.1073/pnas.0808187106

Brevers, D., Bechara, A., Kilts, C., Antoniali, V., Bruylant, A., Verbanck, P., . . . Noël, X. (2017). Competing Motivations: Proactive Response Inhibition Toward Addiction-Related Stimuli in Quitting-Motivated Individuals. *Journal of Gambling Studies, 34*(3), 785-806. doi:10.1007/s10899-017-9722-2

Brevers, D., Cleeremans, A., Verbruggen, F., Bechara, A., Kornreich, C., Verbanck, P., & Noël, X. (2012). Impulsive action but not impulsive choice determines problem gambling severity. *PLoS One, 7*(11), e50647. doi:10.1371/journal.pone.0050647

Campbell, A. E., Chambers, C. D., Allen, C. P. G., Hedge, C., & Sumner, P. (2017). Impairment of manual but not saccadic response inhibition following acute alcohol intoxication. *Drug and Alcohol Dependence, 181*, 242-254. doi:10.1016/j.drugalcdep.2017.08.022

Carbia, C., Lopez-Caneda, E., Corral, M., & Cadaveira, F. (2018). A systematic review of neuropsychological studies involving young binge drinkers. *Neuroscience & Biobehavioral Reviews, 90*, 332-349. doi:10.1016/j.neubiorev.2018.04.013

Cardenas, V. A., Studholme, C., Gazdzinski, S., Durazzo, T. C., & Meyerhoff, D. J. (2007). Deformation-based morphometry of brain changes in alcohol dependence and abstinence. *NeuroImage, 34*(3), 879-887. doi:10.1016/j.neuroimage.2006.10.015

Carey, K. B., Carey, M. P., Maisto, S. A., & Henson, J. M. (2004). Temporal stability of the timeline followback interview for alcohol and drug use with psychiatric outpatients. *Journal of Studies on Alcohol and Drugs, 65*(6), 774-781.

Carter, B. L., & Tiffany, S. T. (1999). Meta-analysis of cue-reactivity in addiction research. *Addiction, 94*(3), 327-340.

Casey, B. J., Trainor, R. J., Orendi, J. L., Schubert, A. B., Nystrom, L. E., Giedd, J. N., . . . Rapoport, J. L. (1997). A Developmental Functional MRI Study of Prefrontal Activation during Performance of a Go-No-Go Task. *Journal of Cognitive Neuroscience, 9*(6), 835-847. doi:10.1162/jocn.1997.9.6.835

Castro-Meneses, L. J., Johnson, B. W., & Sowman, P. F. (2015). The effects of impulsivity and proactive inhibition on reactive inhibition and the go process: insights from vocal and manual stop signal tasks. *Frontiers in Human Neuroscience, 9*, 1-12. doi:10.3389/fnhum.2015.00529

Ceballos, N. A., Giuliano, R. J., Wicha, N. Y. Y., & Graham, R. (2012). Acute stress and event-related potential correlates of attention to alcohol images in social drinkers. *Journal of Studies on Alcohol and Drugs, 73*(5), 761-771. doi:10.15288/jsad.2012.73.761

Chatham, C. H., Frank, M. J., & Munakata, Y. (2009). Pupillometric and behavioral markers of a developmental shift in the temporal dynamics of cognitive control. *Proceedings of the National Academy of Sciences of the United States of America, 106*(14), 5529-5533. doi:10.1073/pnas.0810002106

Christiansen, P., & Bloor, J. F. (2014). Individualised but not general alcohol Stroop predicts alcohol use. *Drug and Alcohol Dependence, 134*, 410-413. doi:https://doi.org/10.1016/j.drugalcdep.2013.10.021

Christiansen, P., Cole, J. C., & Field, M. (2012). Ego depletion increases Ad-Lib alcohol consumption: Investigating cognitive mediators and moderators. *Experimental and Clinical Psychopharmacology, 20*(2), 118-128. doi:10.1037/a0026623

Christiansen, P., Cole, J. C., Goudie, A. J., & Field, M. (2012). Components of behavioural impulsivity and automatic cue approach predict unique variance in hazardous drinking. *Psychopharmacology, 219*(2), 501-510. doi:10.1007/s00213-011-2396-z

Christiansen, P., Jennings, E., & Rose, A. K. (2016). Anticipated effects of alcohol stimulate craving and impair inhibitory control. *Psychology of Addictive Behaviors, 30*(3), 383-388. doi:10.1037/adb0000148

Christiansen, P., Rose, A. K., Cole, J. C., & Field, M. (2013). A comparison of the anticipated and pharmacological effects of alcohol on cognitive bias, executive function, craving and ad-lib drinking. *Journal of Psychopharmacology, 27*(1), 84-92. doi:10.1177/0269881112450787

Christiansen, P., Townsend, G., Knibb, G., & Field, M. (2017). Bibi ergo sum: the effects of a placebo and contextual alcohol cues on motivation to drink alcohol. *Psychopharmacology, 234*(5), 827-835. doi:10.1007/s00213-016-4518-0

Colder, C. R., & O'Connor, R. (2002). Attention bias and disinhibited behavior as predictors of alcohol use and enhancement reasons for drinking. *Psychology of Addictive Behaviors, 16*(4), 325-332. doi:10.1037/0893-164X.16.4.325

Collins, R. L., George, W. H., & Lapp, W. M. (1989). Drinking restraint: Refinement of a construct and prediction of alcohol consumption. *Cognitive Therapy and Research, 13*(5), 423-440. doi:10.1007/bf01173904

Collins, R. L., Koutsky, J. R., & Izzo, C. V. (2000). Temptation, Restriction, and the Regulation of Alcohol Intake: Validity and Utility of the Temptation and Restraint Inventory. *Journal of Studies on Alcohol and Drugs, 61,* 766.

Collins, R. L., & Lapp, W. M. (1992). The Temptation and Restraint Inventory for measuring drinking restraint. *British Journal of Addiction, 87*(4), 625-633.

Compton, W. M., Gfroerer, J., Conway, K. P., & Finger, M. S. (2014). Unemployment and substance outcomes in the United States 2002–2010. *Drug and Alcohol Dependence, 142*, 350-353. doi:https://doi.org/10.1016/j.drugalcdep.2014.06.012

Congdon, E., Mumford, J. A., Cohen, J. R., Galvan, A., Canli, T., & Poldrack, R. A. (2012). Measurement and reliability of response inhibition. *Frontiers in Psychology, 3*, 37. doi:10.3389/fpsyg.2012.00037

Conners, C. K., Epstein, J. N., Angold, A., & Klaric, J. (2003). Continuous Performance Test Performance in a Normative Epidemiological Sample. *Journal of Abnormal Child Psychology, 31*(5), 555-562. doi:10.1023/A:1025457300409

Constantinou, N., Morgan, C. J. A., Battistella, S., O'Ryan, D., Davis, P., & Curran, H. V. (2010). Attentional bias, inhibitory control and acute stress in current and former opiate addicts. *Drug and Alcohol Dependence, 109*(1), 220-225. doi:https://doi.org/10.1016/j.drugalcdep.2010.01.012

Cox, W. M., Brown, M. A., & Rowlands, L. J. (2003). The effects of alcohol cue exposure on non-dependent drinkers' attentional bias for alcohol-related stimuli. *Alcohol and Alcoholism, 38*(1), 45-49. doi:10.1093/alcalc/agg010

Crews, F. T., Braun, C. J., Hoplight, B., Switzer III, R. C., & Knapp, D. J. (2000). Binge Ethanol Consumption Causes Differential Brain Damage in Young Adolescent Rats Compared With Adult Rats. *Alcoholism: Clinical and Experimental Research, 24*(11), 1712-1723. doi:10.1111/j.1530-0277.2000.tb01973.x

Crews, F. T., Collins, M. A., Dlugos, C., Littleton, J., Wilkins, L., Neafsey, E. J., . . . Noronha, A. (2004). Alcohol-induced neurodegeneration: when, where and why? *Alcoholism: Clinical and Experimental Research, 28*(2), 350-364.

Criaud, M., Wardak, C., Ben Hamed, S., Ballanger, B., & Boulinguez, P. (2012). Proactive Inhibitory Control of Response as the Default State of Executive Control. *Frontiers in Psychology, 3*(59). doi:10.3389/fpsyg.2012.00059

Crime survey for England and Wales. (2013-14). Retrieved from https://www.ons.gov.uk/surveys/informationforhouseholdsandindividuals/householdandindividualsurveys/crimesurveyforenglandandwales#targetText=The%20Crime%20Survey%20for%20England%20and%20Wales%20(formerly%20British%20Crime,crime%20in%20England%20and%20Wales.&targetText=the%20criminal%20justice%20system.

Czapla, M., Simon, J. J., Friederich, H. C., Herpertz, S. C., Zimmermann, P., & Loeber, S. (2015). Is binge drinking in young adults associated with an alcohol-specific impairment of response inhibition? *European Addiction Research, 21*(2), 105-113. doi:10.1159/000367939

Czapla, M., Simon, J. J., Richter, B., Kluge, M., Friederich, H. C., Herpertz, S., . . . Loeber, S. (2016). The impact of cognitive impairment and impulsivity on relapse of alcohol-dependent patients: implications for psychotherapeutic treatment. *Addiction Biology, 21*(4), 873-884. doi:10.1111/adb.12229

Dawe, S., & Loxton, N. J. (2004). The role of impulsivity in the development of substance use and eating disorders. *Neuroscience and Biobehavioral Reviews, 28*(3), 343-351. doi:10.1016/j.neubiorev.2004.03.007

de Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: a review of underlying processes. *Addiction Biology, 14*(1), 22-31. doi:10.1111/j.1369-1600.2008.00129.x

de Wit, H., & Chutuape, M. A. (1993). Increased ethanol choice in social drinkers following ethanol preload. *Behavioural Pharmacology, 4*(1), 29-36.

de Wit, H., Crean, J., & Richards, J. B. (2000). Effects of d-amphetamine and ethanol on a measure of behavioral inhibition in humans. *Behavioral Neuroscience, 114*(4), 830-837. doi:10.1037//0735-7044.114.4.830

de Wit, H., Soderpalm, A. H., Nikolayev, L., & Young, E. (2003). Effects of acute social stress on alcohol consumption in healthy subjects. *Alcoholism: Clinical and Experimetal Research, 27*(8), 1270-1277. doi:10.1097/01.Alc.0000081617.37539.D6

Dickerson, S. S., & Kemeny, M. E. (2004). Acute Stressors and Cortisol Responses: A Theoretical Integration and Synthesis of Laboratory Research. *Psychological Bulletin, 130*(3), 355-391. doi:10.1037/0033-2909.130.3.355

Dierolf, A. M., Fechtner, J., Böhnke, R., Wolf, O. T., & Naumann, E. (2017). Influence of acute stress on response inhibition in healthy men: An ERP study. *Psychophysiology, 54*(5), 684-695. doi:10.1111/psyp.12826

Dimoska, A., Johnstone, S. J., & Barry, R. J. (2006). The auditory-evoked N2 and P3 components in the stop-signal task: indices of inhibition, response-conflict or error-detection? *Brain and Cognition, 62*(2), 98-112. doi:10.1016/j.bandc.2006.03.011

Dimoska, A., Johnstone, S. J., Barry, R. J., & Clarke, A. R. (2003). Inhibitory motor control in children with attention-deficit/hyperactivity disorder: event-related potentials in the stop-signal paradigm. *Biological Psychiatry, 54*(12), 1345-1354. doi:https://doi.org/10.1016/S0006-3223(03)00703-0

Donkers, F. C. L., & van Boxtel, G. J. M. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. *Brain and Cognition, 56*(2), 165-176. doi:https://doi.org/10.1016/j.bandc.2004.04.005

Drobes, D. J. (2002). Cue Reactivity in Alcohol and Tobacco Dependence. *Alcoholism: Clinical and Experimental Research, 26*(12), 1928-1929. doi:10.1111/j.1530-0277.2002.tb02506.x

Duka, T., Tasker, R., & Stephens, D. N. (1998). Alcohol choice and outcome expectancies in social drinkers. *Behavioural Pharmacology, 9*(7), 643-653.

Duka, T., & Townshend, J. M. (2004). The priming effect of alcohol pre-load on attentional bias to alcohol-related stimuli. *Psychopharmacology (Berl), 176*(3-4), 353-361. doi:10.1007/s00213-004-1906-7

Durston, S., Thomas, K. M., Yang, Y., Uluğ, A. M., Zimmerman, R. D., & Casey, B. J. (2002). A neural basis for the development of inhibitory control. *Developmental Science, 5*(4), F9-F16. doi:10.1111/1467-7687.00235

Dybek, I., Bischof, G., Grothues, J., Reinhardt, S., Meyer, C., Hapke, U., . . . Rumpf, H.-J. (2006). The Reliability and Validity of the Alcohol Use Disorders Identification Test (AUDIT) in a German General Practice Population Sample. *Journal of Studies on Alcohol, 67*(3), 473-481. doi:10.15288/jsa.2006.67.473

Easdon, C., Izenberg, A., Armilio, M. L., Yu, H., & Alain, C. (2005). Alcohol consumption impairs stimulus- and error-related processing during a Go/No-Go Task. *Brain Research: Cognitive Brain Research, 25*(3), 873-883. doi:10.1016/j.cogbrainres.2005.09.009

Eisenberg, I. W., Bissett, P. G., Zeynep Enkavi, A., Li, J., MacKinnon, D. P., Marsch, L. A., & Poldrack, R. A. (2019). Uncovering the structure of self-regulation through data-driven ontology discovery. *Nature Communications, 10*(1), 2319. doi:10.1038/s41467-019-10301-1

Elchlepp, H., Lavric, A., Chambers, C. D., & Verbruggen, F. (2016). Proactive inhibitory control: A general biasing account. *Cognitive Psychology, 86*, 27-61. doi:10.1016/j.cogpsych.2016.01.004

Enoch, M. A. (2011). The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology (Berl), 214*(1), 17-31. doi:10.1007/s00213-010-1916-6

Enriquez-Geppert, S., Konrad, C., Pantev, C., & Huster, R. J. (2010). Conflict and inhibition differentially affect the N200/P300 complex in a combined go/nogo and stop-signal task. *NeuroImage, 51*(2), 877-887. doi:https://doi.org/10.1016/j.neuroimage.2010.02.043

Ersche, K. D., Jones, P. S., Williams, G. B., Turton, A. J., Robbins, T. W., & Bullmore, E. T. (2012). Abnormal brain structure implicated in stimulant drug addiction. *Science, 335*(6068), 601-604. doi:10.1126/science.1214463

Everitt, B. J. (2014). Neural and psychological mechanisms underlying compulsive drug seeking habits and drug memories – indications for novel treatments of addiction. *European Journal of Neuroscience, 40*(1), 2163-2182. doi:10.1111/ejn.12644

Everitt, B. J., Belin, D., Economidou, D., Pelloux, Y., Dalley, J. W., & Robbins, T. W. (2008). Review. Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 363*(1507), 3125-3135. doi:10.1098/rstb.2008.0089

Everling, S., & Fischer, B. (1998). The antisaccade: a review of basic research and clinical studies. *Neuropsychologia, 36*(9), 885-899. doi:10.1016/s0028-3932(98)00020-7

Fatseas, M., Serre, F., Alexandre, J. M., Debrabant, R., Auriacombe, M., & Swendsen, J. (2015). Craving and substance use among patients with alcohol, tobacco, cannabis or heroin addiction: a comparison of substance- and person-specific cues. *Addiction, 110*(6), 1035-1042. doi:10.1111/add.12882

Fernie, G., Christiansen, P., Cole, J. C., Rose, A. K., & Field, M. (2012). Effects of 0.4g/kg alcohol on attentional bias and alcohol-seeking behaviour in heavy and moderate social drinkers. *Journal of Psychopharmacology, 26*(7), 1017-1025. doi:10.1177/0269881111434621

Fernie, G., Cole, J. C., Goudie, A. J., & Field, M. (2010). Risk-taking but not response inhibition or delay discounting predict alcohol consumption in social drinkers. *Drug and Alcohol Dependence, 112*(1-2), 54-61. doi:10.1016/j.drugalcdep.2010.05.011

Fernie, G., Peeters, M., Gullo, M. J., Christiansen, P., Cole, J. C., Sumnall, H., & Field, M. (2013). Multiple behavioural impulsivity tasks predict prospective alcohol involvement in adolescents. *Addiction, 108*(11), 1916-1923. doi:10.1111/add.12283

Field, M., Christiansen, P., Hardman, C. A., Haynes, A., Jones, A., Robinson, E., & Reid, A. (2019). Translation of laboratory research into behavioral interventions for obesity and problem drinking: The experimental medicine approach. doi:https://doi.org/10.31234/osf.io/scre4

Field, M., Di Lemma, L., Christiansen, P., & Dickson, J. (2017). Automatic avoidance tendencies for alcohol cues predict drinking after detoxification treatment in alcohol dependence. *Psychology of Addictive Behaviors, 31*(2), 171-179. doi:10.1037/adb0000232

Field, M., & Jones, A. (2017). Elevated alcohol consumption following alcohol cue exposure is partially mediated by reduced inhibitory control and increased craving. *Psychopharmacology (Berl)*. doi:10.1007/s00213-017-4694-6

Field, M., Kiernan, A., Eastwood, B., & Child, R. (2008). Rapid approach responses to alcohol cues in heavy drinkers. *Journal of Behavior Therapy and Experimental Psychiatry, 39*(3), 209-218. doi:10.1016/j.jbtep.2007.06.001

Field, M., & Powell, H. (2007). Stress increases attentional bias for alcohol cues in social drinkers who drink to cope. *Alcohol and Alcoholism, 42*(6), 560-566. doi:10.1093/alcalc/agm064

Field, M., & Quigley, M. (2009). Mild stress increases attentional bias in social drinkers who drink to cope: A replication and extension. *Experimental and Clinical Psychopharmacology, 17*(5), 312-319. doi:10.1037/a0017090

Field, M., Werthmann, J., Franken, I., Hofmann, W., Hogarth, L., & Roefs, A. (2016). The role of attentional bias in obesity and addiction. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association, 35*(8), 767-780. doi:10.1037/hea0000405

Field, M., Wiers, R. W., Christiansen, P., Fillmore, M. T., & Verster, J. C. (2010). Acute alcohol effects on inhibitory control and implicit cognition: Implications for loss of control over drinking. *Alcoholism: Clinical and Experimental Research, 34*(8), 1346-1352. doi:10.1111/j.1530-0277.2010.01218.x

Fillmore, M. T. (2003). Drug Abuse as a Problem of Impaired Control: Current Approaches and Findings. *Behavioral and Cognitive Neuroscience Reviews, 2*(3), 179-197. doi:10.1177/1534582303257007

Fillmore, M. T. (2007). Acute alcohol-induced impairment of cognitive functions: Past and present findings. *International Journal on Disability and Human Development, 6*(2), 115-125. doi:10.1515/IJDHD.2007.6.2.115

Fillmore, M. T., Mulvihill, L. E., & Vogel-Sprott, M. (1994). The expected drug and its expected effect interact to determine placebo responses to alcohol and caffeine. *Psychopharmacology (Berl), 115*(3), 383-388.

Fillmore, M. T., Ostling, E. W., Martin, C. A., & Kelly, T. H. (2009). Acute effects of alcohol on inhibitory control and information processing in high and low sensation-seekers. *Drug and Alcohol Dependence, 100*(1), 91-99. doi:https://doi.org/10.1016/j.drugalcdep.2008.09.007

Fillmore, M. T., & Rush, C. R. (2002). Impaired inhibitory control of behavior in chronic cocaine users. *Drug & Alcohol Dependence, 66*(3), 265-273. doi:10.1016/S0376-8716(01)00206-X

Finn, P. R. (2002). Motivation, working memory, and decision making: a cognitive-motivational theory of personality vulnerability to alcoholism. *Behavioral and Cognitive Neuroscience Reviews, 1*(3), 183-205.

Finn, P. R., Justus, A., Mazas, C., & Steinmetz, J. E. (1999). Working memory, executive processes and the effects of alcohol on Go/No-Go learning: testing a model of behavioral regulation and impulsivity. *Psychopharmacology (Berl), 146*(4), 465-472. doi:10.1007/pl00005492

Fleming, K. A., & Bartholow, B. D. (2014). Alcohol Cues, Approach Bias, and Inhibitory Control: Applying a Dual Process Model of Addiction to Alcohol Sensitivity. *Psychology of Addictive Behaviors, 28*(1), 85-96. doi:10.1037/a0031565

Fleming, K. A., Bartholow, B. D., Hilgard, J., McCarthy, D. M., O'Neill, S. E., Steinley, D., & Sher, K. J. (2016). The Alcohol Sensitivity Questionnaire: Evidence for Construct Validity. *Alcoholism: Clinical and Experimetnal Research, 40*(4), 880-888. doi:10.1111/acer.13015

Forrest, W., Hay, C., Widdowson, A. O., & Rocque, M. (2019). Development of impulsivity and risk-seeking: Implications for the dimensionality and stability of self-control. *Criminology, 57*(3), 512-543. doi:10.1111/1745-9125.12214

Franken, I. H. A., Luijten, M., van der Veen, F. M., & van Strien, J. W. (2017). Cognitive control in young heavy drinkers: An ERP study. *Drug and Alcohol Dependence, 175*, 77-83. doi:https://doi.org/10.1016/j.drugalcdep.2017.01.036

Friedman, N. P., & Miyake, A. (2004). The relations among inhibition and interference control functions: a latent-variable analysis. *Journal of Experimental Psychology., 133*(1), 101-135. doi:10.1037/0096-3445.133.1.101

Fromme, K., Stroot, E. A., & Kaplan, D. (1993). Comprehensive effects of alcohol: Development and psychometric assessment of a new expectancy questionnaire. *Psychological Assessment, 5*(1), 19-26. doi:10.1037/1040-3590.5.1.19

Gärtner, A., & Strobel, A. (2019). Individual differences in inhibitory control: A latent variable analysis. doi:10.31234/osf.io/gnhmt

Gauggel, S., Heusinger, A., Forkmann, T., Boecker, M., Lindenmeyer, J., Miles Cox, W., & Staedtgen, M. (2010). Effects of Alcohol Cue Exposure on Response Inhibition in Detoxified Alcohol-Dependent Patients. *Alcoholism: Clinical and Experimental Research, 34*(9), 1584-1589. doi:doi:10.1111/j.1530-0277.2010.01243.x

Gazdzinski, S., Durazzo, T. C., & Meyerhoff, D. J. (2005). Temporal dynamics and determinants of whole brain tissue volume changes during recovery from alcohol dependence. *Drug and Alcohol Dependence, 78*(3), 263-273. doi:https://doi.org/10.1016/j.drugalcdep.2004.11.004

Global Status Report on Alcohol and Health. (2018). Retrieved from https://www.who.int/substance_abuse/publications/global_alcohol_report/en/.

Goldstein, R. Z., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry, 159*(10), 1642-1652. doi:10.1176/appi.ajp.159.10.1642

Gonthier, C., Macnamara, B. N., Chow, M., Conway, A. R. A., & Braver, T. S. (2016). Inducing Proactive Control Shifts in the AX-CPT. *Frontiers in Psychology, 7*, 1822-1822. doi:10.3389/fpsyg.2016.01822

Goudriaan, A. E., Oosterlaan, J., de Beurs, E., & van den Brink, W. (2006). Neurocognitive functions in pathological gambling: a comparison with alcohol dependence, Tourette syndrome and normal controls. *Addiction, 101*(4), 534-547. doi:10.1111/j.1360-0443.2006.01380.x

Grégoire, S., Rivalan, M., Le Moine, C., & Dellu-Hagedorn, F. (2012). The synergy of working memory and inhibitory control: Behavioral, pharmacological and neural functional evidences. *Neurobiology of Learning and Memory, 97*(2), 202-212. doi:https://doi.org/10.1016/j.nlm.2011.12.003

Gullo, M. J., & Stieger, A. A. (2011). Anticipatory stress restores decision-making deficits in heavy drinkers by increasing sensitivity to losses. *Drug and Alcohol Dependence, 117*(2), 204-210. doi:http://dx.doi.org/10.1016/j.drugalcdep.2011.02.002

Hackman, D. A., Farah, M. J., & Meaney, M. J. (2010). Socioeconomic status and the brain: mechanistic insights from human and animal research. *Nature reviews. Neuroscience, 11*(9), 651-659. doi:10.1038/nrn2897

Hagger, M. S., Chatzisarantis, N. L. D., Alberts, H., Anggono, C. O., Batailler, C., Birt, A. R., & Brand, R. (2016). A Multilab Preregistered Replication of the Ego-Depletion Effect. *Perspectives on Psychological Science, 11*(4), 546-573. doi:10.1177/1745691616652873

Hallett, P. E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Research, 18*(10), 1279-1296. doi:10.1016/0042-6989(78)90218-3

Ham, L. S., Stewart, S. H., Norton, P. J., & Hope, D. A. (2005). Psychometric assessment of the comprehensive effects of alcohol questionnaire: Comparing a brief version to the original full scale. *Journal of Psychopathology and Behavioral Assessment, 27*(3), 141-158. doi:10.1007/s10862-005-0631-9

Ham, L. S., Wang, Y., Kim, S. Y., & Zamboanga, B. L. (2013). Measurement Equivalence of the Brief Comprehensive Effects of Alcohol Scale in a Multiethnic Sample of College Students. *Journal of Clinical Psychology, 69*(4), 341-363. doi:10.1002/jclp.21904

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. *NeuroImage, 50*(3), 1313-1319. doi:10.1016/j.neuroimage.2009.12.109

Hanson, D. J. (Ed.) (2013). *Historical evolution of alcohol consumption in society*. Oxford: University Press.

Hatzenbuehler, M. L., Corbin, W. R., & Fromme, K. (2008). Trajectories and determinants of alcohol use among LGB young adults and their heterosexual peers: results from a prospective study. *Developmental Psychology, 44*(1), 81-90. doi:10.1037/0012-1649.44.1.81

Health Matters: Harmful Drinking and Alcohol Dependence. (2016). Retrieved from https://www.gov.uk/government/publications/health-matters-harmful-drinking-and-alcohol-dependence/health-matters-harmful-drinking-and-alcohol-dependence.

Hellhammer, D. H., Wüst, S., & Kudielka, B. M. (2009). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology, 34*(2), 163-171.

Henderson, R. K., Snyder, H. R., Gupta, T., & Banich, M. T. (2012). When does stress help or harm? The effects of stress controllability and subjective stress response on stroop performance. *Frontiers in Psychology, 3*, 179-179. doi:10.3389/fpsyg.2012.00179

Herman, A. M., Critchley, H. D., & Duka, T. (2018). Risk-Taking and Impulsivity: The Role of Mood States and Interoception. *Frontiers in Psychology, 9*, 1625-1625. doi:10.3389/fpsyg.2018.01625

Hermans, E. J., Henckens, M. J., Joels, M., & Fernandez, G. (2014). Dynamic adaptation of large-scale brain networks in response to acute stressors. *Trends in Neuroscience, 37*(6), 304-314. doi:10.1016/j.tins.2014.03.006

Herrmann, M. J., Weijers, H. G., Wiesbeck, G. A., Böning, J., & Fallgatter, A. J. (2001). Alcohol cue-reactivity in heavy and light social drinkers as revealed by event-related potentials *Alcohol and Alcoholism, 36*(6), 588-593. doi:10.1093/alcalc/36.6.588

Hesselbrock, V., Begleiter, H., Porjesz, B., O'Connor, S., & Bauer, L. (2001). P300 event-related potential amplitude as an endophenotype of alcoholism--evidence from the collaborative study on the genetics of alcoholism. *Journal of Biomedical Sciences, 8*(1), 77-82. doi:54016

Hoeppner, B. B., Stout, R. L., Jackson, K. M., & Barnett, N. P. (2010). How good is fine-grained Timeline Follow-back data? Comparing 30-day TLFB and repeated 7-day TLFB alcohol consumption reports on the person and daily level. *Addictive Behaviors, 35*(12), 1138-1143. doi:10.1016/j.addbeh.2010.08.013

Hofmann, W., Schmeichel, B. J., & Baddeley, A. D. (2012). Executive functions and self-regulation. *Trends in Cognitive Sciences, 16*(3), 174-180. doi:10.1016/j.tics.2012.01.006

Houston, R. J., Derrick, J. L., Leonard, K. E., Testa, M., Quigley, B. M., & Kubiak, A. (2014). Effects of heavy drinking on executive cognitive functioning in a community sample. *Addictive Behaviors, 39*(1), 345-349.

Hu, S., Ide, J. S., Zhang, S., Sinha, R., & Li, C.-s. R. (2015). Conflict anticipation in alcohol dependence — A model-based fMRI study of stop signal task. *Neuroimage: Clinical, 8*, 39-50. doi:https://doi.org/10.1016/j.nicl.2015.03.008

Hu, S., Zhang, S., Chao, H. H., Krystal, J. H., & Li, C.-S. R. (2016). Association of Drinking Problems and Duration of Alcohol Use to Inhibitory Control in Nondependent Young Adult Social Drinkers. *Alcoholism: Clinical and Experimental Research, 40*(2), 319-328. doi:10.1111/acer.12964

Huster, R. J., Enriquez-Geppert, S., Lavallee, C. F., Falkenstein, M., & Herrmann, C. S. (2013). Electroencephalography of response inhibition tasks: Functional networks and cognitive contributions. *International Journal of Psychophysiology, 87*(3), 217-233. doi:https://doi.org/10.1016/j.ijpsycho.2012.08.001

Hutchenson, G., & Sofroniou, N. (1999). *The Multivatiate Social Scientist*. London: Sage.

Jahfari, S., Stinear, C. M., Claffey, M., Verbruggen, F., & Aron, A. R. (2010). Responding with restraint: what are the neurocognitive mechanisms? *Journal of Cognitive Neuroscience, 22*(7), 1479-1492. doi:10.1162/jocn.2009.21307

Jones, A., Baines, L., Ruddock, H., Franken, I., Verbruggen, F., & Field, M. (2019). Does alcohol cue Inhibitory Control Training survive a context shift? doi:https://doi.org/10.31234/osf.io/tzbjm

Jones, A., Button, E., Rose, A. K., Robinson, E., Christiansen, P., Di Lemma, L., & Field, M. (2016). The ad-libitum alcohol 'taste test': secondary analyses of potential confounds and construct validity. *Psychopharmacology, 233*, 917-924. doi:10.1007/s00213-015-4171-z

Jones, A., Christiansen, P., Nederkoorn, C., Houben, K., & Field, M. (2013). Fluctuating Disinhibition: Implications for the Understanding and Treatment of Alcohol and Other Substance Use Disorders. *Frontiers in Psychiatry, 4*(140). doi:10.3389/fpsyt.2013.00140

Jones, A., Di Lemma, L. C. G., Robinson, E., Christiansen, P., Nolan, S., Tudur-Smith, C., & Field, M. (2016). Inhibitory control training for appetitive behaviour change: A meta-analytic investigation of mechanisms of action and moderators of effectiveness. *Appetite, 97*, 16-28. doi:https://doi.org/10.1016/j.appet.2015.11.013

Jones, A., & Field, M. (2015). Alcohol-related and negatively valenced cues increase motor and oculomotor disinhibition in social drinkers. *Experimental and Clinical Psychopharmacology, 23*(2), 122-129. doi:10.1037/pha0000011

Jones, A., Field, M., Christiansen, P., & Stancak, A. (2013). P300 during response inhibition is associated with ad-lib alcohol consumption in social drinkers. *Journal of Psychopharmacology, 27*(6), 507-514. doi:10.1177/0269881113485142

Jones, A., McGrath, E., Robinson, E., Houben, K., Nederkoorn, C., & Field, M. (2018). A randomized controlled trial of inhibitory control training for the reduction of alcohol consumption in problem drinkers. *Journal of Consulting and Clinical Psychology, 86*(12), 991-1004. doi:10.1037/ccp0000312

Jones, A., Robinson, E., Duckworth, J., Kersbergen, I., Clarke, N., & Field, M. (2018). The effects of exposure to appetitive cues on inhibitory control: A meta-analytic investigation. *Appetite, 128*, 271-282. doi:10.1016/j.appet.2018.06.024

Jones, A., Rose, A. K., Cole, J., & Field, M. (2013). Effects of Alcohol Cues on Craving and Ad Libitum Alcohol Consumption in Social Drinkers: The Role of Disinhibition. *Journal of Experimental Psychopathology, 4*(3), 239-249. doi:10.5127/jep.031912

Jones, A., Tiplady, B., Houben, K., Nederkoorn., & Field. (2018). Do daily fluctuations in inhibitory control predict alcohol consumption? An ecological momentary assessment study. *Psychopharmacology, 235*(5), 1487-1496. doi:10.1007/s00213-018-4860-5

Julian, L. J. (2011). Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care and Research, 63* S467-472. doi:10.1002/acr.20561

Kaiser, H. (1960). The Application of Electronic Computers to Factor Analysis. *Educational and Psychological Measurement, 20*(1), 141-151. doi:10.1177/001316446002000116
Kamarajan, C., Porjesz, B., Jones, K. A., Choi, K., Chorlian, D. B., Padmanabhapillai, A., . . . Begleiter, H. (2005). Alcoholism is a disinhibitory disorder: neurophysiological evidence from a Go/No-Go task. *Biological Psychology, 69*(3), 353-373. doi:https://doi.org/10.1016/j.biopsycho.2004.08.004
Kaplan, R. M., & Irvin, V. L. (2015). Likelihood of Null Effects of Large NHLBI Clinical Trials Has Increased over Time. *PLOS ONE, 10*(8), e0132382. doi:10.1371/journal.pone.0132382
Kareken, D. A., Dzemidzic, M., Wetherill, L., Eiler, W., 2nd, Oberlin, B. G., Harezlak, J., . . . O'Connor, S. J. (2013). Family history of alcoholism interacts with alcohol to affect brain regions involved in behavioral inhibition. *Psychopharmacology, 228*(2), 335-345. doi:10.1007/s00213-013-3038-4
Kaupuzs, A., Vazne, Z., & Usca, S. (2015). Evaluation of Psychometric Properties of the State and Trait Anxiety Inventory Scale in a Student Sample. *Proceedings of the International Scientific Conference*. doi:10.17770/sie2015vol1.317
King, A., Munisamy, G., de Wit, H., & Lin, S. (2006). Attenuated cortisol response to alcohol in heavy social drinkers. *International Journal of Psychophysiology, 59*(3), 203-209. doi:10.1016/j.ijpsycho.2005.10.008
Klein, A., & Anker, J. (2013). A Psychometric Evaluation of the Approach and Avoidance of Alcohol Questionnaire Among Alcohol-Dependent Patients Attending Residential Treatment. *Journal of Psychopathology and Behavioral Assessment, 35*(2), 205-214. doi:10.1007/s10862-012-9322-5
Kline, P. (1999). *Handbook of Psychological Testing*. London: Routledge.
Knibb, G., Roberts, C. A., Robinson, E., Rose, A., & Christiansen, P. (2018). The effect of beliefs about alcohol's acute effects on alcohol priming and alcohol-induced impairments of inhibitory control. *PLOS ONE, 13*(7), e0201042. doi:10.1371/journal.pone.0201042
Kok, A., Ramautar, J. R., De Ruiter, M. B., Band, G. P. H., & Ridderinkhof, K. R. (2004). ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology, 41*(1), 9-20. doi:10.1046/j.1469-8986.2003.00127.x
Kokkonen, M., & Pulkkinen, L. (2001). Examination of the paths between personality, current mood, its evaluation, and emotion regulation. *European Journal of Personality, 15*(2), 83-104. doi:10.1002/per.397
Koob, G. F., & Volkow, N. D. (2010). Neurocircuitry of addiction. *Neuropsychopharmacology, 35*(1), 217-238. doi:10.1038/npp.2009.110
Koordeman, R., Anschutz, D. J., & Engels, R. C. M. E. (2011). Exposure to Alcohol Commercials in Movie Theaters Affects Actual Alcohol Consumption in Young Adult High Weekly Drinkers: An Experimental Study. *The American Journal on Addictions, 20*(3), 285-291. doi:doi:10.1111/j.1521-0391.2011.00134.x
Kreek, M. J., Nielsen, D. A., Butelman, E. R., & LaForge, K. S. (2005). Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction. *Nature Neuroscience, 8*(11), 1450-1457. doi:10.1038/nn1583
Kreusch, F., Quertemont, E., Vilenne, A., & Hansenne, M. (2014). Alcohol abuse and ERP components in Go/No-go tasks using alcohol-related stimuli: Impact of alcohol avoidance. *International Journal of Psychophysiology, 94*(1), 92-99. doi:https://doi.org/10.1016/j.ijpsycho.2014.08.001
Kreusch, F., Vilenne, A., & Quartemont, E. (2013). Response inhibition toward alcohol-related cues using an alcohol go/no-go task in problem and non-problem drinkers. *Addictive Behaviors, 38*(10), 2520-2528.

Kreusch, F., Vilenne, A., & Quertemont, E. (2013). Response inhibition toward alcohol-related cues using an alcohol go/no-go task in problem and non-problem drinkers. *Addictive Behaviors, 38*(10), 2520-2528. doi:10.1016/j.addbeh.2013.04.007
Kubota, M., Nakazaki, S., Hirai, S., Saeki, N., Yamaura, A., & Kusaka, T. (2001). Alcohol consumption and frontal lobe shrinkage: study of 1432 non-alcoholic subjects. *Journal of Neurology, Neurosurgery & Psychiatry, 71*(1), 104. doi:10.1136/jnnp.71.1.104
Lavagnino, L., Arnone, D., Cao, B., Soares, J. C., & Selvaraj, S. (2016). Inhibitory control in obesity and binge eating disorder: A systematic review and meta-analysis of neurocognitive and neuroimaging studies. *Neuroscience and Biobehavioral Reviews, 68*, 714-726. doi:10.1016/j.neubiorev.2016.06.041
Lawrence, A. J., Luty, J., Bogdan, N. A., Sahakian, B. J., & Clark, L. (2009). Impulsivity and response inhibition in alcohol dependence and problem gambling. *Psychopharmacology, 207*(1), 163-172. doi:10.1007/s00213-009-1645-x
Lee, M. R., Bartholow, B. D., McCarthy, D. M., Pedersen, S. L., & Sher, K. J. (2015). Two alternative approaches to conventional person-mean imputation scoring of the Self-Rating of the Effects of Alcohol Scale (SRE). *Psychology of Addictive Behaviors 29*(1), 231-236. doi:10.1037/adb0000015
Leeman, R. F., Corbin, W. R., & Fromme, K. (2009). Craving predicts within session drinking behavior following placebo. *Personality and Individual Differences, 46*(7), 693-698. doi:10.1016/j.paid.2009.01.024
Lejuez, C. W., Aklin, W. M., Zvolensky, M. J., & Pedulla, C. M. (2003). Evaluation of the Balloon Analogue Risk Task (BART) as a predictor of adolescent real-world risk-taking behaviours. *Journal of Adolescence, 26*(4), 475-479. doi:10.1016/S0140-1971(03)00036-8
Lesh, T. A., Westphal, A. J., Niendam, T. A., Yoon, J. H., Minzenberg, M. J., Ragland, J. D., . . . Carter, C. S. (2013). Proactive and reactive cognitive control and dorsolateral prefrontal cortex dysfunction in first episode schizophrenia. *Neuroimage: Clinical, 2*, 590-599. doi:10.1016/j.nicl.2013.04.010
Lewis, M. (2017). Addiction and the Brain: Development, Not Disease. *Neuroethics, 10*(1), 7-18. doi:10.1007/s12152-016-9293-4
Li, C.-s. R., & Sinha, R. (2008). Inhibitory control and emotional stress regulation: Neuroimaging evidence for frontal–limbic dysfunction in psycho-stimulant addiction. *Neuroscience & Biobehavioral Reviews, 32*(3), 581-597. doi:https://doi.org/10.1016/j.neubiorev.2007.10.003
Lijffijt, M., Bekker, E. M., Quik, E. H., Bakker, J., Kenemans, J. L., & Verbaten, M. N. (2004). Differences between low and high trait impulsivity are not associated with differences in inhibitory motor control. *Journal of Attention Disorders, 8*(1), 25-32. doi:10.1177/108705470400800104
Littel, M., Euser, A. S., Munafo, M. R., & Franken, I. H. (2012). Electrophysiological indices of biased cognitive processing of substance-related cues: a meta-analysis. *Neuroscience and Biobehavioral Reviews, 36*(8), 1803-1816. doi:10.1016/j.neubiorev.2012.05.001
Littlefield, A. K., Sher, K. J., & Wood, P. K. (2010). Do changes in drinking motives mediate the relation between personality change and "maturing out" of problem drinking? *Journal of Abnormal Psychology, 119*(1), 93-105. doi:10.1037/a0017512
Littman, R., & Takacs, A. (2017). Do all inhibitions act alike? A study of go/no-go and stop-signal paradigms. *PLoS One, 12*(10), e0186774. doi:10.1371/journal.pone.0186774
Liu, Y., van den Wildenberg, W. P. M., de Graaf, Y., Ames, S. L., Baldacchino, A., Bo, R., . . .

Wiers, R. W. (2019). Is (poly-) substance use associated with impaired inhibitory control? A mega-analysis controlling for confounders. *Neuroscience and Biobehavioural Reviews,105, 288-304. doi:10.1016/j.neubiorev.2019.07.006*

Liu, Y., Zhan, X., Li, W., Han, H., Wang, H., Hou, J., . . . Wang, Y. (2015). The trait anger affects conflict inhibition: a Go/Nogo ERP study. *Frontiers in Human Neuroscience, 8*, 1076-1076. doi:10.3389/fnhum.2014.01076

Local Alcohol Profiles for England: March 2017. (2017). Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/596268/LAPE_March_2017_statistical_commentary.pdf.

Local Health and Care Planning: Menu of preventative interventions. (2016). Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/683016/Local_health_and_care_planning_menu_of_preventative_interventions_DM_NICE_amends_14.02.18__2_.pdf

Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological Review, 91*(3), 295-327. doi:10.1037/0033-295X.91.3.295

Logan, G. D., Cowan, W. B., & Davis, K. A. (1984). On the ability to inhibit simple and choice reaction time responses: A model and a method. *Journal of Experimental Psychology: Human Perception and Performance, 10*(2), 276-291. doi:10.1037/0096-1523.10.2.276

Lopez-Caneda, E., Cadaveira, F., Crego, A., Gomez-Suarez, A., Corral, M., Parada, M., . . . Rodriguez Holguin, S. (2012). Hyperactivation of right inferior frontal cortex in young binge drinkers during response inhibition: a follow-up study. *Addiction, 107*(10), 1796-1808. doi:10.1111/j.1360-0443.2012.03908.x

López-Caneda, E., Rodríguez Holguín, S., Cadaveira, F., Corral, M., & Doallo, S. (2013). Impact of Alcohol Use on Inhibitory Control (and Vice Versa) During Adolescence and Young Adulthood: A Review. *Alcohol and Alcoholism, 49*(2), 173-181. doi:10.1093/alcalc/agt168

Luethi, M., Meier, B., & Sandi, C. (2008). Stress effects on working memory, explicit memory, and implicit memory for neutral and emotional stimuli in healthy men. *Frontiers in Behavioral Neuroscience, 2*, 5. doi:10.3389/neuro.08.005.2008

Luijten, M., Littel, M., & Franken, I. H. A. (2011). Deficits in Inhibitory Control in Smokers During a Go/NoGo Task: An Investigation Using Event-Related Brain Potentials. *PLOS ONE, 6*(4), e18898. doi:10.1371/journal.pone.0018898

Lukasik, K. M., Waris, O., Soveri, A., Lehtonen, M., & Laine, M. (2019). The Relationship of Anxiety and Stress With Working Memory Performance in a Large Non-depressed Sample. *Frontiers in Psychology, 10*(4). doi:10.3389/fpsyg.2019.00004

Luna, B., Thulborn, K. R., Munoz, D. P., Merriam, E. P., Garver, K. E., Minshew, N. J., . . . Sweeney, J. A. (2001). Maturation of Widely Distributed Brain Function Subserves Cognitive Development. *NeuroImage, 13*(5), 786-793. doi:https://doi.org/10.1006/nimg.2000.0743

Lyvers, M., Hasking, P., Hani, R., Rhodes, M., & Trew, E. (2010). Drinking motives, drinking restraint and drinking behaviour among young adults. *Addictive Behaviors, 35*(2), 116-122. doi:https://doi.org/10.1016/j.addbeh.2009.09.011

MacKillop, J., & Lisman, S. A. (2007). Examining the effect of perceived availability on craving for alcohol: A quasi-experimental approach. *Addiction Research & Theory, 15*(3), 231-245. doi:10.1080/16066350701407104

MacKillop, J., Lisman, S. A., & Weinstein, A. (2006). Psychometric Validation of the Temptation and Restraint Inventory in Two Samples of College Drinkers. *Journal of*

Psychopathology and Behavioral Assessment, 28(3), 157-163. doi:10.1007/s10862-005-9000-y

Madden, G. J., Petry, N. M., Badger, G. J., & Bickel, W. K. (1997). Impulsive and self-control choices in opioid-dependent patients and non-drug-using control participants: drug and monetary rewards. *Experimental and Clinical Psychopharmacology, 5*(3), 256-262.

Magrys, S. A., & Olmstead, M. C. (2015). Acute Stress Increases Voluntary Consumption of Alcohol in Undergraduates. *Alcohol and Alcoholism, 50*(2), 213-218. doi:10.1093/alcalc/agu101

Mahedy, L., Field, M., Gage, S., Hammerton, G., Heron, J., Hickman, M., & Munafò, M. R. (2018). Alcohol Use in Adolescence and Later Working Memory: Findings From a Large Population-Based Birth Cohort. *Alcohol and Alcoholism, 53*(3), 251-258. doi:10.1093/alcalc/agx113

Mahmood, O. M., Goldenberg, D., Thayer, R., Migliorini, R., Simmons, A. N., & Tapert, S. F. (2013). Adolescents' fMRI activation to a response inhibition task predicts future substance use. *Addictive Behaviors, 38*(1), 1435-1441. doi:10.1016/j.addbeh.2012.07.012

Mainz, V., Drüke, B., Boecker, M., Kessel, R., Gauggel, S., & Forkmann, T. (2012). Influence of cue exposure on inhibitory control and brain activation in patients with alcohol dependence. *Frontiers in Human Neuroscience, 6*, 92. doi:10.3389/fnhum.2012.00092

Mann, K., Ackermann, K., Croissant, B., Mundle, G., Nakovics, H., & Diehl, A. (2005). Neuroimaging of Gender Differences in Alcohol Dependence: Are Women More Vulnerable? *Alcoholism: Clinical and Experimental Research, 29*(5), 896-901. doi:10.1097/01.Alc.0000164376.69978.6b

Marczinski, C. A., Abroms, B. D., Van Selst, M., & Fillmore, M. T. (2005). Alcohol-induced impairment of behavioral control: Differential effects on engaging vs. disengaging responses. *Psychopharmacology, 182*(3), 452-459. doi:10.1007/s00213-005-0116-2

Marlatt, G. A., Demming, B., & Reid, J. B. (1973). Loss of control drinking in alcoholics: an experimental analogue. *Journal of Abnormal Psychology, 81*(3), 233-241.

Martinez, D., Broft, A., Foltin, R. W., Slifstein, M., Hwang, D., Huang, Y., . . . Laruelle, M. (2004). Cocaine Dependence and D2 Receptor Availability in the Functional Subdivisions of the Striatum: Relationship with Cocaine-Seeking Behavior. *Neuropsychopharmacology, 29*(6), 1190-1202. doi:10.1038/sj.npp.1300420

Martinez, D., Narendran, R., Foltin, R. W., Slifstein, M., Hwang, D., Broft, A., . . . Laruelle, M. (2007). Amphetamine-Induced Dopamine Release: Markedly Blunted in Cocaine Dependence and Predictive of the Choice to Self-Administer Cocaine. *American Journal of Psychiatry, 164*(4), 622-629. doi:10.1176/ajp.2007.164.4.622

Matta, A. d., Gonçalves, F. L., & Bizarro, L. (2012). Delay discounting: Concepts and measures. *Psychology & Neuroscience, 5*(2), 135-146. doi:10.3922/j.psns.2012.2.03

Mayer, J. D., Allen, J. P., & Beauregard, K. (1995). Mood inductions for four specific moods: A procedure employing guided imagery vignettes with music. US: Brandon House.

Mayer, J. D., & Gaschke, Y. N. (1988). The experience and meta-experience of mood. *Journal of Personality and Social Psychology, 55*(1), 102-111. doi:10.1037/0022-3514.55.1.102

McEvoy, P. M., Stritzke, W. G. K., French, D. J., Lang, A. R., & Ketterman, R. L. (2004). Comparison of three models of alcohol craving in young adults: A cross-validation. *Addiction, 99*(4), 482-497.

McGrath, E., Jones, A., & Field, M. (2016). Acute stress increases ad-libitum alcohol consumption in heavy drinkers, but not through impaired inhibitory control. *Psychopharmacology, 233*(7), 1227-1234. doi:10.1007/s00213-016-4205-1

Metzger, R. (1976). A reliability and validity study of the State-Trait Anxiety Inventory. *Journal of Clinical Psychology, 32*(2), 276-278. doi:10.1002/1097-4679(197604)32:23.0.CO;2-G

Meule, A. (2017). Reporting and Interpreting Task Performance in Go/No-Go Affective Shifting Tasks. *Frontiers in Psychology, 8*(701). doi:10.3389/fpsyg.2017.00701

Mirsky, J. B., Heuer, H. W., Jafari, A., Kramer, J. H., Schenk, A. K., Viskontas, I. V., . . . Boxer, A. L. (2011). Anti-saccade performance predicts executive function and brain structure in normal elders. *Cognitive and Behavioral Neuroloy, 24*(2), 50-58. doi:10.1097/WNN.0b013e318223f6c6

Miyake, A., & Friedman, N. (2012). The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. *Current Directions in Psychological Science, 21*, 8-14. doi:10.1177/0963721411429458

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The Unity and Diversity of Executive Functions and Their Contributions to Complex "Frontal Lobe" Tasks: A Latent Variable Analysis. *Cognitive Psychology, 41*(1), 49-100. doi:https://doi.org/10.1006/cogp.1999.0734

Moeller, S. J., Bederson, L., Alia-Klein, N., & Goldstein, R. Z. (2016). Neuroscience of inhibition for addiction medicine: from prediction of initiation to prediction of relapse. *Progress in Brain Research, 223*, 165-188. doi:10.1016/bs.pbr.2015.07.007

Monk, R. L., Sunley, J., Qureshi, A. W., & Heim, D. (2016). Smells like inhibition: The effects of olfactory and visual alcohol cues on inhibitory control. *Psychopharmacology, 233*(8), 1331-1337. doi:10.1007/s00213-016-4221-1

Monterosso, J. R., Aron, A. R., Cordova, X., Xu, J., & London, E. D. (2005). Deficits in response inhibition associated with chronic methamphetamine abuse. *Drug and Alcohol Dependence, 79*(2), 273-277. doi:10.1016/j.drugalcdep.2005.02.002

Montoya, A. K., & Hayes, A. F. (2016). Two-Condition Within-Participant Statistical Mediation Analysis: A Path-Analytic Framework. *Psychological Methods*. doi:10.1037/met0000086

Morein-Zamir, S., & Robbins, T. W. (2015). Fronto-striatal circuits in response-inhibition: Relevance to addiction. *Brain Research, 1628*, 117-129. doi:10.1016/j.brainres.2014.09.012

Moreno, M., Estevez, A. F., Zaldivar, F., Montes, J. M. G., Gutiérrez-Ferre, V. E., Esteban, L., . . . Flores, P. (2012). Impulsivity differences in recreational cannabis users and binge drinkers in a university population. *Drug and Alcohol Dependence, 124*(3), 355-362. doi:https://doi.org/10.1016/j.drugalcdep.2012.02.011

Munafò, M. R., Nosek, B. A., Bishop, D. V. M., Button, K. S., Chambers, C. D., Percie du Sert, N., . . . Ioannidis, J. P. A. (2017). A manifesto for reproducible science. *Nature Human Behaviour, 1*(1), 0021. doi:10.1038/s41562-016-0021

Munakata, Y., Herd, S. A., Chatham, C. H., Depue, B. E., Banich, M. T., & O'Reilly, R. C. (2011). A unified framework for inhibitory control. *Trends in Cognitive Sciences, 15*(10), 453-459. doi:https://doi.org/10.1016/j.tics.2011.07.011

Muraven, M., & Shmueli, D. (2006). The self-control costs of fighting the temptation to drink. *Psychology of Addictive Behaviors, 20*(2), 154-160. doi:10.1037/0893-164X.20.2.154

Murphy, P. (2002). Inhibitory control in adults with Attention-Deficit/Hyperactivity Disorder. *Journal of Attention Disorders, 6*(1), 1-4. doi:10.1177/108705470200600101

Murphy, P., & Garavan, H. (2011). Cognitive predictors of problem drinking and AUDIT scores among college students. *Drug and Alcohol Dependence, 115*(1-2), 94-100. doi:10.1016/j.drugalcdep.2010.10.011

Namkoong, K., Lee, E., Lee, C. H., Lee, B. O., & An, S. K. (2004). Increased P3 amplitudes induced by alcohol-related pictures in patients with alcohol dependence. *Alcoholism: Clinical and Experimental Research, 28*(9), 1317-1323. doi:10.1097/01.alc.0000139828.78099.69

National Confidential Inquiry into Suicide and Homicide by People with Mental Illness. (2015). Retrieved from https://sites.manchester.ac.uk/ncish/

Nederkoorn, C., Baltus, M., Guerrieri, R., & Wiers, R. W. (2009). Heavy drinking is associated with deficient response inhibition in women but not in men. *Pharmacology Biochemistry and Behavior, 93*(3), 331-336. doi:10.1016/j.pbb.2009.04.015

Nederkoorn, C., Smulders, F. T., Havermans, R. C., Roefs, A., & Jansen, A. (2006). Impulsivity in obese women. *Appetite, 47*(2), 253-256. doi:10.1016/j.appet.2006.05.008

Newman, J. P., & Kosson, D. S. (1986). Passive avoidance learning in psychopathic and nonpsychopathic offenders. *Journal of Abnormal Psychology, 95*(3), 252-260.

Nigg, J. T., Wong, M. M., Martel, M. M., Jester, J. M., Puttler, L. I., Glass, J. M., . . . Zucker, R. A. (2006). Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(4), 468-475. doi:10.1097/01.chi.0000199028.76452.a9

Nixon, K., & Crews, F. T. (2002). Binge ethanol exposure decreases neurogenesis in adult rat hippocampus. *Journal of Neurochemistry, 83*(5), 1087-1093. doi:10.1046/j.1471-4159.2002.01214.x

Noël, X., Paternot, J., Van der Linden, M., Sferrazza, R., Verhas, M., Hanak, C., . . . Verbanck, P. (2001). Correlation between inhibition, working memory and delimited frontal area blood flow measure by 99mTc-Bicisate SPECT in alcohol-dependent patients. *Alcohol and Alcoholism, 36*(6), 556-563. doi:10.1093/alcalc/36.6.556

Noël, X., Van der Linden, M., d'Acremont, M., Bechara, A., Dan, B., Hanak, C., & Verbanck, P. (2007). Alcohol cues increase cognitive impulsivity in individuals with alcoholism. *Psychopharmacology (Berl), 192*(2), 291-298. doi:10.1007/s00213-006-0695-6

Norman, L. J., Taylor, S. F., Liu, Y., Radua, J., Chye, Y., De Wit, S. J., . . . Fitzgerald, K. (2019). Error Processing and Inhibitory Control in Obsessive-Compulsive Disorder: A Meta-analysis Using Statistical Parametric Maps. *Biological Psychiatry, 85*(9), 713-725. doi:10.1016/j.biopsych.2018.11.010

Nosek, B. A., Ebersole, C. R., DeHaven, A. C., & Mellor, D. T. (2018). The preregistration revolution. *Proceedings of the National Academy of Sciences, 115*(11), 2600. doi:10.1073/pnas.1708274114

Oddy, B. W., & Barry, R. J. (2009). The relationship of N2 and P3 to inhibitory processing of social drinkers in a Go/NoGo task. *International Journal of Psychophysiology 72*(3), 323-330. doi:10.1016/j.ijpsycho.2009.02.002

Oei, N. Y., Everaerd, W. T., Elzinga, B. M., van Well, S., & Bermond, B. (2006). Psychosocial stress impairs working memory at high loads: an association with cortisol levels and memory retrieval. *Stress, 9*(3), 133-141. doi:10.1080/10253890600965773

Oppenheimer, D. M., Meyvis, T., & Davidenko, N. (2009). Instructional manipulation checks: Detecting satisficing to increase statistical power. *Journal of Experimental Social Psychology, 45*(4), 867-872. doi:https://doi.org/10.1016/j.jesp.2009.03.009

Ortner, C. N. M., MacDonald, T. K., & Olmstead, M. C. (2003). Alcohol intoxication reduces impulsivity in the Delay-discounting paradigm. *Alcohol and Alcoholism, 38*(2), 151-156. doi:10.1093/alcalc/agg041

Owens, M. M., Ray, L. A., & MacKillop, J. (2015). Behavioral economic analysis of stress effects on acute motivation for alcohol. *Journal of the Experimental Analysis of Behavior, 103*(1), 77-86. doi:10.1002/jeab.114

Pandey, A. K., Kamarajan, C., Tang, Y., Chorlian, D. B., Roopesh, B. N., Manz, N., . . . Porjesz, B. (2012). Neurocognitive deficits in male alcoholics: an ERP/sLORETA analysis of the N2 component in an equal probability Go/NoGo task. *Biological Psychology, 89*(1), 170-182. doi:10.1016/j.biopsycho.2011.10.009

Papachristou, H., Nederkoorn, C., Corstjens, J., & Jansen, A. (2012). The role of impulsivity and perceived availability on cue-elicited craving for alcohol in social drinkers. *Psychopharmacology, 224*(1), 145-153. doi:10.1007/s00213-012-2747-4

Papachristou, H., Nederkoorn, C., Havermans, R., van der Horst, M., & Jansen, A. (2012). Can't stop the craving: The effect of impulsivity on cue-elicited craving for alcohol in heavy and light social drinkers. *Psychopharmacology, 219*(2), 511-518. doi:10.1007/s00213-011-2240-5

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt Impulsiveness Scale. *Journal of Clinical Psychology, 51*(6), 768-774.

Paxton, J. L., Barch, D. M., Racine, C. A., & Braver, T. S. (2008). Cognitive control, goal maintenance, and prefrontal function in healthy aging. *Cerebral Cortex, 18*(5), 1010-1028. doi:10.1093/cercor/bhm135

Paz, A. L., Keim, C. A., & Rosselli, M. (2016). Inhibitory Performance Predicting Drinking Behaviours Among Young Adults. *Alcohol and Alcoholism, 51*(6), 677-683. doi:10.1093/alcalc/agw017

Peeters, M., Janssen, T., Monshouwer, K., Boendermaker, W., Pronk, T., Wiers, R., & Vollebergh, W. (2015). Weaknesses in executive functioning predict the initiating of adolescents' alcohol use. *Developmental Cognitive Neuroscience, 16*, 139-146. doi:https://doi.org/10.1016/j.dcn.2015.04.003

Perry, J. L., & Carroll, M. E. (2008). The role of impulsive behavior in drug abuse. *Psychopharmacology (Berl), 200*(1), 1-26. doi:10.1007/s00213-008-1173-0

Petersen, I. T., Hoyniak, C. P., McQuillan, M. E., Bates, J. E., & Staples, A. D. (2016). Measuring the development of inhibitory control: The challenge of heterotypic continuity. *Developmental Review, 40*, 25-71. doi:10.1016/j.dr.2016.02.001

Petit, G., Kornreich, C., Noël, X., Verbanck, P., & Campanella, S. (2012). Alcohol-related context modulates performance of social drinkers in a visual Go/No-Go task: a preliminary assessment of event-related potentials. *PLoS One, 7*(5), e37466. doi:10.1371/journal.pone.0037466

Petrides, M., & Milner, B. (1982). Deficits on subject-ordered tasks after frontal- and temporal-lobe lesions in man. *Neuropsychologia, 20*(3), 249-262. doi:https://doi.org/10.1016/0028-3932(82)90100-2

Pfefferbaum, A., Sullivan, E. V., Mathalon, D. H., & Lim, K. O. (1997). Frontal lobe volume loss observed with magnetic resonance imaging in older chronic alcoholics. *Alcoholism: Clinical and Experimental Research, 21*(3), 521-529. doi:10.1111/j.1530-0277.1997.tb03798.x

Plawecki, M. H., Koskie, S., Kosobud, A., Justiss, M. D., & O'Connor, S. (2018). Alcohol intoxication progressively impairs drivers' capacity to detect important environmental stimuli. *Pharmacology, Biochemistry and Behavior, 175*, 62-68. doi:https://doi.org/10.1016/j.pbb.2018.05.009

Pomerleau, O. F., Fertig, J., Baker, L., & Cooney, N. (1983). Reactivity to alcohol cues in alcoholics and non-alcoholics: Implications for a stimulus control analysis of drinking. *Addictive Behaviors, 8*(1), 1-10. doi:https://doi.org/10.1016/0306-4603(83)90048-5

Quinn, P. D., & Fromme, K. (2011). Subjective response to alcohol challenge: a quantitative review. *Alcoholism: Clinical and Experimental Research, 35*(10), 1759-1770. doi:10.1111/j.1530-0277.2011.01521.x

Rae, C. L., Hughes, L. E., Weaver, C., Anderson, M. C., & Rowe, J. B. (2014). Selection and stopping in voluntary action: a meta-analysis and combined fMRI study. *NeuroImage, 86*(100), 381-391. doi:10.1016/j.neuroimage.2013.10.012

Ratcliff, R., & Smith, P. L. (2004). A comparison of sequential sampling models for two-choice reaction time. *Psychological Review, 111*(2), 333-367. doi:10.1037/0033-295x.111.2.333

Redick, T. S. (2014). Cognitive control in context: Working memory capacity and proactive control. *Acta Psychologica, 145*(1), 1-9. doi:10.1016/j.actpsy.2013.10.010

Redick, T. S., & Engle, R. W. (2011). Rapid communication: Integrating working memory capacity and context-processing views of cognitive control. *Quarterly Journal of Experimental Psychology, 64*(6), 1048-1055. doi:10.1080/17470218.2011.577226

Reichenberg, L. W. (2013). *DSM-5 Essentials : The Savvy Clinician's Guide to the Changes in Criteria*. New York, United States: John Wiley & Sons, Incorporated.

Reis, J., Harned, I., & Riley, W. (2004). Young Adult's Immediate Reaction to a Personal Alcohol Overdose. *Journal of Drug Education, 34*(3), 235-245. doi:10.2190/NY8N-D7D7-PVF8-MLCU

Reynolds, B., Ortengren, A., Richards, J. B., & de Wit, H. (2006). Dimensions of impulsive behavior: Personality and behavioral measures. *Personality and Individual Differences, 40*(2), 305-315. doi:https://doi.org/10.1016/j.paid.2005.03.024

Reynolds, B., Richards, J. B., & de Wit, H. (2006). Acute-alcohol effects on the Experiential Discounting Task (EDT) and a question-based measure of delay discounting. *Pharmacology Biochemistry and Behavior, 83*(2), 194-202. doi:10.1016/j.pbb.2006.01.007

Richards, J. B., Zhang, L., Mitchell, S. H., & de Wit, H. (1999). Delay or probability discounting in a model of impulsive behavior: effect of alcohol. *Journal of the Experimental Analysis of Behavior, 71*(2), 121-143. doi:10.1901/jeab.1999.71-121

Richmond, L. L., Redick, T. S., & Braver, T. S. (2015). Remembering to Prepare: The Benefits (and Costs) of High Working Memory Capacity. *Journal of Experimental Psychology: Learning Memory and Cognition, 41*(6), 1764-1777. doi:10.1037/xlm0000122

Riggs, N. R., & Pentz, M. A. (2016). Inhibitory control and the onset of combustible cigarette, e-cigarette, and hookah use in early adolescence: The moderating role of socioeconomic status. *Child Neuropsychology, 22*(6), 679-691. doi:10.1080/09297049.2015.1053389

Roberts, W., Miller, M. A., Weafer, J., & Fillmore, M. T. (2014). Heavy drinking and the role of inhibitory control of attention. *Experimental and Clinical Psychopharmacology, 22*(2), 133-140. doi:10.1037/a0035317

Robinson, S. M., Sobell, L. C., Sobell, M. B., & Leo, G. I. (2014). Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychology of Addictive Behaviors, 28*(1), 154-162. doi:10.1037/a0030992

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Research Reviews, 18*(3), 247-291. doi:https://doi.org/10.1016/0165-0173(93)90013-P

Robinson, T. E., & Berridge, K. C. (2008). The incentive sensitization theory of addiction: some current issues. *Philosophical Transactions of the Royal Society of London, 363*(1507), 3137-3146. doi:10.1098/rstb.2008.0093

Roos, L. E., Knight, E. L., Beauchamp, K. G., Berkman, E. T., Faraday, K., Hyslop, K., & Fisher, P. A. (2017). Acute stress impairs inhibitory control based on individual differences in parasympathetic nervous system activity. *Biological Psychology, 125*, 58-63. doi:http://dx.doi.org/10.1016/j.biopsycho.2017.03.004

Rose, A. K., & Duka, T. (2008). Effects of alcohol on inhibitory processes. *Behavioural Pharmacology, 19*(4), 284-291. doi:10.1097/FBP.0b013e328308f1b2

Rose, A. K., & Grunsell, L. (2008). The subjective, rather than the disinhibiting, effects of alcohol are related to binge drinking. *Alcoholism: Clinical and Experimental Research, 32*(6), 1096-1104. doi:10.1111/j.1530-0277.2008.00672.x

Rose, A. K., Hobbs, M., & Drummond, C. (2013). Differentiating the Contribution of Pharmacological from Alcohol Expectancy Effects to Changes in Subjective Response and Priming Over Successive Drinks. *Alcoholism: Clinical and Experimental Research, 37*(4), 687-695. doi:doi:10.1111/acer.12022

Rosenberg, G., Bauld, L., Hooper, L., Buykx, P., Holmes, J., & Vohra, J. (2017). New national alcohol guidelines in the UK: public awareness, understanding and behavioural intentions. *Journal of Public Health, 40*(3), 549-556. doi:10.1093/pubmed/fdx126

Rosvold, H. E., Mirsky, A. F., Sarason, I., Bransome Jr, E. D., & Beck, L. H. (1956). A continuous performance test of brain damage. *Journal of Consulting Psychology, 20*(5), 343-350. doi:10.1037/h0043220

Rubia, K., Smith, A. B., Brammer, M. J., & Taylor, E. (2003). Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. *Neuroimage, 20*(1), 351-358.

Rubio, G., Jimenez, M., Rodriguez-Jimenez, R., Martinez, I., Avila, C., Ferre, F., . . . Palomo, T. (2008). The role of behavioral impulsivity in the development of alcohol dependence: a 4-year follow-up study. *Alcoholism: Clinical and Experimental Research, 32*(9), 1681-1687. doi:10.1111/j.1530-0277.2008.00746.x

Rueger, S., Trela, C., Palmeri, M., & C King, A. (2012). Self-Administered Web-Based Timeline Followback Procedure for Drinking and Smoking Behaviors in Young Adults. *Journal of Studies on Alcohol and Drugs, 73*(5), 829-833. doi:10.15288/jsad.2012.73.829

Rupp, C. I., Beck, J. K., Heinz, A., Kemmler, G., Manz, S., Tempel, K., & Fleischhacker, W. W. (2016). Impulsivity and Alcohol Dependence Treatment Completion: Is There a Neurocognitive Risk Factor at Treatment Entry? *Alcoholism: Clinical and Experimental Research, 40*(1), 152-160. doi:doi:10.1111/acer.12924

Rush, B. K., Barch, D. M., & Braver, T. S. (2006). Accounting for cognitive aging: context processing, inhibition or processing speed? *Neuropsychology, Development, and Cognition., 13*(3-4), 588-610. doi:10.1080/13825580600680703

Russell, M., Cooper, M. L., Frone, M. R., & Peirce, R. S. (1999). A longitudinal study of stress, alcohol, and blood pressure in community-based samples of blacks and non-blacks. *Alcohol Research & Health, 23*(4), 299-306.

Saliasi, E., Geerligs, L., Lorist, M. M., & Maurits, N. M. (2013). The relationship between P3 amplitude and working memory performance differs in young and older adults. *PLoS One, 8*(5), e63701. doi:10.1371/journal.pone.0063701

Saunders, B., Milyavskaya, M., Etz, A., Randles, D., & Inzlicht, M. (2018). Reported self-control is not meaningfully associated with inhibition-related executive function: A Bayesian analysis. *Collabra: Psychology, 4*(1).

Saunders, J. B., Aasland, O. G., Babor, T. F., De la Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption II. *Addiction, 88*(6), 791-804.

Schäfer, T., & Schwarz, M. A. (2019). The Meaningfulness of Effect Sizes in Psychological Research: Differences Between Sub-Disciplines and the Impact of Potential Biases. *Frontiers in Psychology, 10*(813). doi:10.3389/fpsyg.2019.00813

Scholz, U., La Marca, R., Nater, U. M., Aberle, I., Ehlert, U., Hornung, R., . . . Kliegel, M. (2009). Go no-go performance under psychosocial stress: Beneficial effects of implementation intentions. *Neurobiology of Learning and Memory, 91*(1), 89-92. doi:http://dx.doi.org/10.1016/j.nlm.2008.09.002

Schoofs, D., Preuss, D., & Wolf, O. T. (2008). Psychosocial stress induces working memory impairments in an n-back paradigm. *Psychoneuroendocrinology, 33*(5), 643-653. doi:10.1016/j.psyneuen.2008.02.004

Schuckit, M. A., & Smith, T. L. (1996). An 8-year follow-up of 450 sons of alcoholic and control subjects. *Archives of General Psychiatry, 53*(3), 202-210. doi:10.1001/archpsyc.1996.01830030020005

Schuckit, M. A., & Smith, T. L. (2000). The Relationships of a Family History of Alcohol Dependence, a Low Level of Response to Alcohol and Six Domains of Life Functioning to the Development of Alcohol Use Disorders. *Journal of Studies on Alcohol, 61*(6), 827-835.

Schuckit, M. A., Smith, T. L., Kalmijn, J., Tsuang, J., Hesselbrock, V., & Bucholz, K. (2000). Response to Alcohol in Daughters of Alcoholics: A Pilot Study and a Comparison with Sons of Alcoholics. *Alcohol and Alcoholism, 35*(3), 242-248. doi:10.1093/alcalc/35.3.242

Schuckit, M. A., Smith, T. L., Trim, R. S., Allen, R. C., Fukukura, T., Knight, E. E., . . . Kreikebaum, S. A. (2011). A prospective evaluation of how a low level of response to alcohol predicts later heavy drinking and alcohol problems. *The American Journal of Drug and Alcohol Abuse, 37*(6), 479-486. doi:10.3109/00952990.2011.598590

Schwabe, L., Hoffken, O., Tegenthoff, M., & Wolf, O. T. (2013). Stress-induced enhancement of response inhibition depends on mineralocorticoid receptor activation. *Psychoneuroendocrinology, 38*(10), 2319-2326. doi:10.1016/j.psyneuen.2013.05.001

Serre, F., Fatseas, M., Swendsen, J., & Auriacombe, M. (2015). Ecological momentary assessment in the investigation of craving and substance use in daily life: a systematic review. *Drug and Alcohol Dependence, 148*, 1-20. doi:10.1016/j.drugalcdep.2014.12.024

Sharma, D. (2017). The variable nature of cognitive control in a university sample of young adult drinkers. *Journal of Applied Social Psychology, 47*(3), 118-123. doi:10.1111/jasp.12416

Shealy, A. E., Murphy, J. G., Borsari, B., & Correia, C. J. (2007). Predictors of motivation to change alcohol use among referred college students. *Addictive Behaviors, 32*(10), 2358-2364. doi:10.1016/j.addbeh.2007.02.003

Shields, A. L., Guttmannova, K., & Caruso, J. C. (2004). An examination of the factor structure of the Alcohol Use Disorders Identification Test in two high-risk samples. *Substance Use & Misuse, 39*(7), 1161-1182.

Sinha, R. (2001). How does stress increase risk of drug abuse and relapse? *Psychopharmacology (Berl), 158*(4), 343-359. doi:10.1007/s002130100917

Smith, J. L., Dash, N. J., Johnstone, S. J., Houben, K., & Field, M. (2017). Current forms of inhibitory training produce no greater reduction in drinking than simple assessment: A

preliminary study. *Drug and Alcohol Dependence, 173*, 47-58. doi:10.1016/j.drugalcdep.2016.12.018

Smith, J. L., Iredale, J. M., & Mattick, R. P. (2016). Sex differences in the relationship between heavy alcohol use, inhibition and performance monitoring: Disconnect between behavioural and brain functional measures. *Psychiatry Research: Neuroimaging, 254*, 103-111. doi:10.1016/j.pscychresns.2016.06.012

Smith, J. L., & Mattick, R. P. (2018). Are there sex differences in the relationship between heavy alcohol use and disinhibition? A meta-analysis.

Smith, J. L., Mattick, R. P., Jamadar, S. D., & Iredale, J. M. (2014). Deficits in behavioural inhibition in substance abuse and addiction: a meta-analysis. *Drug and Alcohol Dependence, 145*, 1-33. doi:10.1016/j.drugalcdep.2014.08.009

Sobell, L. C., Brown, J., Leo, G. I., & Sobell, M. B. (1996). The reliability of the Alcohol Timeline Followback when administered by telephone and by computer. *Drug and Alcohol Dependence, 42*(1), 49-54.

Sobell, L. C., & Sobell, M. B. (1990). Self-report issues in alcohol abuse: State of the art and future directions. *Behavioral Assessment, 12*(1), 77-90.

Spielberger, C. D., Sydeman, S. J., Owen, A. E., & Marsh, B. J. (1999). Measuring anxiety and anger with the State-Trait Anxiety Inventory (STAI) and the State-Trait Anger Expression Inventory (STAXI). In *The use of psychological testing for treatment planning and outcomes assessment, 2nd ed.* (pp. 993-1021). Mahwah, NJ, US: Lawrence Erlbaum Associates.

Spitoni, G. F., Ottaviani, C., Petta, A. M., Zingaretti, P., Aragona, M., Sarnicola, A., & Antonucci, G. (2017). Obesity is associated with lack of inhibitory control and impaired heart rate variability reactivity and recovery in response to food stimuli. *International Journal of Psychophysiology, 116*, 77-84. doi:https://doi.org/10.1016/j.ijpsycho.2017.04.001

Squeglia, L. M., Jacobus, J., Nguyen-Louie, T. T., & Tapert, S. F. (2014). Inhibition during early adolescence predicts alcohol and marijuana use by late adolescence. *Neuropsychology, 28*(5), 782-790. doi:10.1037/neu0000083

Stacy, A. W., & Wiers, R. W. (2010). Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annual Review of Clinical Psychology, 6*, 551-575. doi:10.1146/annurev.clinpsy.121208.131444

Stanford, M. S., Mathias, C. W., Dougherty, D. M., Lake, S. L., Anderson, N. E., & Patton, J. H. (2009). Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Differences, 47*(5), 385-395. doi:https://doi.org/10.1016/j.paid.2009.04.008

Starcke, K., Wiesen, C., Trotzke, P., & Brand, M. (2016). Effects of Acute Laboratory Stress on Executive Functions. *Frontiers in Psychology, 7*, 461. doi:10.3389/fpsyg.2016.00461

Statistics on Alcohol, England. (2017). Retrieved from https://www.gov.uk/government/statistics/statistics-on-alcohol-england-2017.

Statistics on Alcohol, England. (2018). Retrieved from https://www.gov.uk/government/statistics/statistics-on-alcohol-england-2018.

Stein, M., Fey, W., Koenig, T., Oehy, J., & Moggi, F. (2018). Context-Specific Inhibition is Related to Craving in Alcohol Use Disorders: A Dangerous Imbalance. *Alcoholism: Clinical and Experimental Research, 42*(1), 69-80. doi:10.1111/acer.13532

Stevens, J. P. (2009). *Applied Multivariate Statistics for the Social Sciences*. New York, NY, US: Routledge.

Swaen, G., Teggeler, O., & van Amelsvoort, L. (2001). False positive outcomes and design characteristics in occupational cancer epidemiology studies. *International Journal of Epidemiology, 30*(5), 948-954. doi:10.1093/ije/30.5.948

Tamm, L., Menon, V., & Reiss, A. L. (2002). Maturation of brain function associated with response inhibition. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*(10), 1231-1238. doi:10.1097/00004583-200210000-00013

Tarter, R. E., Kirisci, L., Habeych, M., Reynolds, M., & Vanyukov, M. (2004). Neurobehavior disinhibition in childhood predisposes boys to substance use disorder by young adulthood: direct and mediated etiologic pathways. *Drug and Alcohol Dependence, 73*(2), 121-132. doi:https://doi.org/10.1016/j.drugalcdep.2003.07.004

Taylor, E. M., Murphy, A., Boyapati, V., Ersche, K. D., Flechais, R., Kuchibatla, S., . . . Platform, I. (2016). Impulsivity in abstinent alcohol and polydrug dependence: a multidimensional approach. *Psychopharmacology, 233*(8), 1487-1499. doi:10.1007/s00213-016-4245-6

Teesson, M., Hall, W., Proudfoot, H., & Degenhardt, L. (2012). *Addictions.* London: Psychology Press.

Testa, M., Fillmore, M. T., Norris, J., Abbey, A., Curtin, J. J., Leonard, K. E., . . . Hayman, L. W., Jr. (2006). Understanding alcohol expectancy effects: revisiting the placebo condition. *Alcoholism: Clinical and Experimental Research, 30*(2), 339-348. doi:10.1111/j.1530-0277.2006.00039.x

Thomas, S. E., Bacon, A. K., Randall, P. K., Brady, K. T., & See, R. E. (2011). An acute psychosocial stressor increases drinking in non-treatment-seeking alcoholics. *Psychopharmacology, 218*(1), 19-28. doi:10.1007/s00213-010-2163-6

Thomas, S. E., Drobes, D. J., & Deas, D. (2005). Alcohol cue reactivity in alcohol-dependent adolescents. *Journal of Studies on Alcohol and Drugs, 66*(3), 354-360.

Thush, C., Wiers, R. W., Ames, S. L., Grenard, J. L., Sussman, S., & Stacy, A. W. (2008). Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. *Drug and Alcohol Dependence, 94*(1-3), 116-124. doi:10.1016/j.drugalcdep.2007.10.019

Tiffany, S. T. (1990). A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. *Psychological Review, 97*(2), 147-168.

Tillman, C. M., Thorell, L. B., Brocki, K. C., & Bohlin, G. (2008). Motor response inhibition and execution in the stop-signal task: development and relation to ADHD behaviors. *Child Neuropsychology, 14*(1), 42-59. doi:10.1080/09297040701249020

Townshend, J. M., & Duka, T. (2001). Attentional bias associated with alcohol cues: differences between heavy and occasional social drinkers. *Psychopharmacology (Berl), 157*(1), 67-74.

van der Plas, E. A. A., Crone, E. A., van den Wildenberg, W. P. M., Tranel, D., & Bechara, A. (2009). Executive control deficits in substance-dependent individuals: a comparison of alcohol, cocaine, and methamphetamine and of men and women. *Journal of Clinical and Experimental Neuropsychology, 31*(6), 706-719. doi:10.1080/13803390802484797

van Holst, R. J., de Ruiter, M. B., van den Brink, W., Veltman, D. J., & Goudriaan, A. E. (2012). A voxel-based morphometry study comparing problem gamblers, alcohol abusers, and healthy controls. *Drug and Alcohol Dependence, 124*(1-2), 142-148. doi:10.1016/j.drugalcdep.2011.12.025

van Velzen, L. S., Vriend, C., de Wit, S. J., & van den Heuvel, O. A. (2014). Response inhibition and interference control in obsessive-compulsive spectrum disorders. *Frontiers in Human Neuroscience, 8*, 419-419. doi:10.3389/fnhum.2014.00419

Veilleux, J. C., & Skinner, K. D. (2015). Smoking, food, and alcohol cues on subsequent behavior: a qualitative systematic review. *Clinical Psychology Review, 36*, 13-27. doi:10.1016/j.cpr.2015.01.001

Verbruggen, F., Aron, A. R., Band, G., Beste, C., Bissett, P., Brockett, A. T., & Boehler, C. N. (2019). A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. *eLife, 8*, e46323. doi:https://doi.org/10.7554/eLife.46323

Verbruggen, F., Best, M., Bowditch, W. A., Stevens, T., & McLaren, I. P. L. (2014). The inhibitory control reflex. *Neuropsychologia, 65*, 263-278. doi:10.1016/j.neuropsychologia.2014.08.014

Verbruggen, F., Chambers, C. D., & Logan, G. D. (2013). Fictitious Inhibitory Differences: How Skewness and Slowing Distort the Estimation of Stopping Latencies. *Psychological Science, 24*(3), 352-362. doi:10.1177/0956797612457390

Verbruggen, F., & De Houwer, J. (2007). Do emotional stimuli interfere with response inhibition? Evidence from the stop signal paradigm. *Cognition and Emotion, 21*(2), 391-403. doi:10.1080/02699930600625081

Verbruggen, F., Liefooghe, B., Notebaert, W., & Vandierendonck, A. (2005). Effects of stimulus–stimulus compatibility and stimulus–response compatibility on response inhibition. *Acta Psychologica, 120*(3), 307-326. doi:https://doi.org/10.1016/j.actpsy.2005.05.003

Verbruggen, F., Liefooghe, B., & Vandierendonck, A. (2006). The effect of interference in the early processing stages on response inhibition in the stop signal task. *The Quarterly Journal of Experimental Psychology, 59*(1), 190-203. doi:10.1080/17470210500151386

Verbruggen, F., & Logan, G. D. (2008). Automatic and controlled response inhibition: associative learning in the go/no-go and stop-signal paradigms. *Journal of Experimental Psychology, 137*(4), 649-672. doi:10.1037/a0013170

Verbruggen, F., & Logan, G. D. (2009a). Models of Response Inhibition in the Stop-Signal and Stop-Change Paradigms. *Neuroscience and Biobehavioral Reviews, 33*(5), 647-661. doi:10.1016/j.neubiorev.2008.08.014

Verbruggen, F., & Logan, G. D. (2009b). Proactive adjustments of response strategies in the stop-signal paradigm. *Journal of Experimental Psychology: Human Perception and Performance, 35*(3), 835-854. doi:10.1037/a0012726

Verbruggen, F., Logan, G. D., & Stevens, M. A. (2008). STOP-IT: Windows executable software for the stop-signal paradigm. *Behavior Research Methods, 40*(2), 479-483. doi:10.3758/brm.40.2.479

Verbruggen, F., McLaren, I. P. L., & Chambers, C. D. (2014). Banishing the Control Homunculi in Studies of Action Control and Behavior Change. *Perspectives on Psychological Science, 9*(5), 497-524. doi:10.1177/1745691614526414

Verbruggen, F., Stevens, T., & Chambers, C. D. (2014). Proactive and reactive stopping when distracted: An attentional account. *Journal of Experimental Psychology: Human Perception and Performance, 40*(4), 1295-1300. doi:10.1037/a0036542

Verdejo-García, A., Lawrence, A. J., & Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience & Biobehavioral Reviews, 32*(4), 777-810. doi:https://doi.org/10.1016/j.neubiorev.2007.11.003

Volkow, N. D., Fowler, J. S., Wolf, A. P., Schlyer, D., Shiue, C. Y., Alpert, R., . . . et al. (1990). Effects of chronic cocaine abuse on postsynaptic dopamine receptors. *The American Journal of Psychiatry, 147*(6), 719-724. doi:10.1176/ajp.147.6.719

Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic Advances from the Brain Disease Model of Addiction. *New England Journal of Medicine, 374*(4), 363-371. doi:10.1056/NEJMra1511480

Volkow, N. D., Wang, G. J., Tomasi, D., & Baler, R. D. (2013). Obesity and addiction: neurobiological overlaps. *Obesity Reviews, 14*(1), 2-18. doi:10.1111/j.1467-789X.2012.01031.x

von Diemen, L., Bassani, D., Fuchs, S., Maciel Szobot, C., & Pechansky, F. (2008). Impulsivity, age of first alcohol use and substance use disorders among male adolescents: a population based case-control study. *Addiction 103*, 1198-1205. doi:10.1111/j.1360-0443.2008.02223.x

Von Gunten, C. D., Bartholow, B. D., & Martins, J. S. (2019). Inhibition tasks are not associated with self-regulation outcomes in healthy college students. doi:https://doi.org/10.31234/osf.io/uwbdg

Watson, T. D., Newton-Mora, M., & Pirkle, J. (2016). Event-related potential correlates of processing alcohol-related pictures in young adult binge drinkers. *The American Journal of Drug and Alcohol Abuse, 42*(1), 77-87. doi:10.3109/00952990.2015.1099660

Weafer, J., & Fillmore, M. T. (2008). Individual differences in acute alcohol impairment of inhibitory control predict ad libitum alcohol consumption. *Psychopharmacology, 201*(3), 315-324. doi:10.1007/s00213-008-1284-7

Weafer, J., & Fillmore, M. T. (2012). Alcohol-related stimuli reduce inhibitory control of behavior in drinkers. *Psychopharmacology (Berl), 222*(3), 489-498. doi:10.1007/s00213-012-2667-3

Weafer, J., & Fillmore, M. T. (2015). Alcohol-related cues potentiate alcohol impairment of behavioral control in drinkers. *Psychology of Addictive Behaviors, 29*(2), 290-299. doi:10.1037/adb0000013

Weafer, J., & Fillmore, M. T. (2016). Low-Dose Alcohol Effects on Measures of Inhibitory Control, Delay Discounting, and Risk-Taking. *Current Addiction Reports, 3*(1), 75-84. doi:10.1007/s40429-016-0086-y

Weafer, J., Mitchell, S. H., & de Wit, H. (2014). Recent Translational Findings on Impulsivity in Relation to Drug Abuse. *Current Addiction Reports, 1*(4), 289-300. doi:10.1007/s40429-014-0035-6

Weissenborn, R., & Duka, T. (2003). Acute alcohol effects on cognitive function in social drinkers: their relationship to drinking habits. *Psychopharmacology (Berl), 165*(3), 306-312. doi:10.1007/s00213-002-1281-1

Wessel, J. R., & Aron, A. R. (2015). It's not too late: The onset of the frontocentral P3 indexes successful response inhibition in the stop-signal paradigm. *Psychophysiology, 52*(4), 472-480. doi:10.1111/psyp.12374

West, R. (2001). Theories of addiction. *Addiction, 96*(1), 3-13. doi:10.1046/j.1360-0443.2001.96131.x

Wiemers, E. A., & Redick, T. S. (2018). Working memory capacity and intra-individual variability of proactive control. *Acta Psychologica, 182*, 21-31. doi:10.1016/j.actpsy.2017.11.002

Wiers, R. W., Bartholow, B. D., van den Wildenberg, E., Thush, C., Engels, R. C., Sher, K. J., . . . Stacy, A. W. (2007). Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. *Pharmacology, Biochemistry, and Behavior, 86*(2), 263-283. doi:10.1016/j.pbb.2006.09.021

Wiers, R. W., Rinck, M., Kordts, R., Houben, K., & Strack, F. (2010). Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. *Addiction, 105*(2), 279-287. doi:10.1111/j.1360-0443.2009.02775.x

Williams, B. R., Ponesse, J. S., Schachar, R. J., Logan, G. D., & Tannock, R. (1999). Development of inhibitory control across the life span. *Developmental Psychology, 35*(1), 205-213.

Wojnar, M., Ilgen, M. A., Czyz, E., Strobbe, S., Klimkiewicz, A., Jakubczyk, A., . . . Brower, K. J. (2009). Impulsive and non-impulsive suicide attempts in patients treated for alcohol dependence. *Journal of Affective Disorders, 115*(1), 131-139. doi:10.1016/j.jad.2008.09.001

Wong, A. L., Goldsmith, J., Forrence, A. D., Haith, A. M., & Krakauer, J. W. (2017). Reaction times can reflect habits rather than computations. *eLife, 6*, e28075. doi:10.7554/eLife.28075

Wong, M. M., Nigg, J. T., Zucker, R. A., Puttler, L. I., Fitzgerald, H. E., Jester, J. M., . . . Adams, K. (2006). Behavioral control and resiliency in the onset of alcohol and illicit drug use: a prospective study from preschool to adolescence. *Child Development, 77*(4), 1016-1033. doi:10.1111/j.1467-8624.2006.00916.x

Woods, D. L., Wyma, J. M., Yund, E. W., Herron, T. J., & Reed, B. (2015). Factors influencing the latency of simple reaction time. *Frontiers in Human Neuroscience, 9*, 131-131. doi:10.3389/fnhum.2015.00131

Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: conflict monitoring and the error-related negativity. *Psychological Review, 111*(4), 931-959. doi:10.1037/0033-295x.111.4.931

Yucel, M., Oldenhof, E., Ahmed, S. H., Belin, D., Billieux, J., Bowden-Jones, H., . . . Verdejo-Garcia, A. (2019). A transdiagnostic dimensional approach towards a neuropsychological assessment for addiction: an international Delphi consensus study. *Addiction, 114*(6), 1095-1109. doi:10.1111/add.14424

Zack, M., Woodford, T. M., Tremblay, A. M., Steinberg, L., Zawertailo, L. A., & Busto, U. E. (2011). Stress and alcohol cues exert conjoint effects on go and stop signal responding in male problem drinkers. *Neuropsychopharmacology, 36*(2), 445-458. doi:10.1038/npp.2010.177

Zago-Gomes Mda, P., & Nakamura-Palacios, E. M. (2009). Cognitive components of frontal lobe function in alcoholics classified according to Lesch's typology. *Alcohol and Alcoholism, 44*(5), 449-457. doi:10.1093/alcalc/agp043

Zahr, N. M., & Pfefferbaum, A. (2017). Alcohol's Effects on the Brain: Neuroimaging Results in Humans and Animal Models. *Alcohol research: Current Reviews, 38*(2), 183-206.

Zamboanga, B. L., Ham, L. S., Olthuis, J. V., Martens, M. P., Grossbard, J. R., & Van Tyne, K. (2012). Alcohol Expectancies and Risky Drinking Behaviors Among High School Athletes: “I’d Rather Keep My Head in the Game”. *Prevention Science, 13*(2), 140-149. doi:10.1007/s11121-011-0252-3

Zandbelt, B. B., Van Buuren, M., Kahn, R. S., & Vink, M. (2011). Reduced proactive inhibition in schizophrenia is related to corticostriatal dysfunction and poor working memory. *Biological Psychiatry, 70*(12), 1151-1158. doi:10.1016/j.biopsych.2011.07.028

Appendices

Appendices 1 Questionnaires.

Appendices 1.A: Alcohol Use Disorders Identification Test (AUDIT).

1) How often do you have a drink containing alcohol?

Never Less than monthly 2-4 times a month 2-3 times per week 4+per week

2) How many drinks containing alcohol do you have on a typical day when you're drinking?

1-2 3-4 5-6 7-9 10+

3) How often do you have 6 or more drinks on one occasion?

Never Less than monthly Monthly Weekly Daily or almost daily

4) How often during the last year have you found that you were not able to stop drinking once you had started?

Never Less than monthly Monthly Weekly Daily or almost daily

5) How often during the last year have you failed to do what was normally expected from you because of drinking?

Never Less than monthly Monthly Weekly Daily or almost daily

6) How often during the last year have you needed a drink first thing in the morning to get yourself going after a heavy drinking session?

Never Less than monthly Monthly Weekly Daily or almost daily

7) How often during the last year have you had a feeling of guilt or remorse after drinking?

Never Less than monthly Monthly Weekly Daily or almost daily

8) How often during the last year have you been unable to remember what happened the night before because you had been drinking?

Never Less than monthly Monthly Weekly Daily or almost daily

9) Have you or someone else been injured because of your drinking?

No Yes, but not in the last year Yes, during the last year

10) Has a relative, friend, doctor or other health worker been concerned about your drinking or suggested you cut down?

No Yes, but not in the last year Yes, during the last year

Appendices 1.B Timeline Follow Back (TLFB)

To help me evaluate your drinking I need to get an idea of your alcohol consumption in the past fourteen days. Please fill out the table with the number of units of alcohol consumed on each day, being as accurate as possible. Please use the information given below to work out how many units you consumed on each day in the past week and fill in the number of units in the table. On days when you did not drink please write 0 (zero). I realise it isn't easy to recall things with 100% accuracy, but if you are not sure how many units you drank on a certain day please try to give it your best guess.

What is a unit of alcohol?

The list below shows the number of units of alcohol in common drinks:-

- A pint of ordinary strength lager (Carling Black Label, Fosters) - 2 units
- A pint of strong lager (Stella Artois, Kronenbourg 1664) - 3 units
- A pint of ordinary bitter (John Smith's, Boddingtons) - 2 units
- A pint of best bitter (Fuller's ESB, Young's Special) - 3 units
- A pint of ordinary strength cider (Woodpecker) - 2 units
- A pint of strong cider (Dry Blackthorn, Strongbow) - 3 units
- A 175ml glass of red or white wine - around 2 units
- A 750ml bottle of red or white wine – around 9 units
- A pub measure of spirits - 1 unit
- An alcopop (eg Smirnoff Ice, Bacardi Breezer, WKD, Reef) - around 1.5 units

Please now fill in the following table stating the total number of alcohol units you consumed for each day. Please start from whichever day it was yesterday and work backwards. For example if today is Monday start from Sunday and work backwards, with Monday being Monday a week ago. Please double check that you have filled in the number of units for all fourteen days.

Last week:

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

Previous week:

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

Appendices 1.C Brief Comprehensive Effects of Alcohol Questionnaire

1. **When I drink alcohol I would feel brave and daring**

1 2 3 4

Disagree Agree

2. **When I drink alcohol It would be easier to talk to people**

1 2 3 4

Disagree Agree

3. **When I drink alcohol I would act sociable**

1 2 3 4

Disagree Agree

4. **When I drink alcohol I would take risks**

1 2 3 4

Disagree Agree

5. **When I drink alcohol I would feel courageous**

1 2 3 4

Disagree Agree

6. **When I drink alcohol I would be loud, boisterous and noisy**

1 2 3 4

Disagree Agree

7. **When I drink alcohol I would feel guilty**

1 2 3 4

Disagree Agree

8. **When I drink alcohol I would feel dizzy**

1 2 3 4

Disagree Agree

9. When I drink alcohol I would feel moody

1 2 3 4

Disagree Agree

10. When I drink alcohol I would be clumsy

1 2 3 4

Disagree Agree

11. When I drink alcohol I would be a better lover

1 2 3 4

Disagree Agree

12. When I drink alcohol I would enjoy sex more

1 2 3 4

Disagree Agree

13. When I drink alcohol I would feel aggressive

1 2 3 4

Disagree Agree

14. When I drink alcohol I would feel peaceful

1 2 3 4

Disagree Agree

15. When I drink alcohol I would feel calm

1	2	3	4
Disagree			Agree

2.1. **When I drink alcohol I would feel brave and daring. This would be...**

1	2	3	4	5
Bad				Good

2.2. When I drink alcohol It would be easier to talk to people. This would be...

1	2	3	4	5
Bad				Good

2.3. When I drink alcohol I would act sociable. This would be...

1	2	3	4	5
Bad				Good

2.4. When I drink alcohol I would take risks. This would be..."

1	2	3	4	5
Bad				Good

2.5. When I drink alcohol I would feel courageous. This would be..."

1	2	3	4	5
Bad				Good

2.6. When I drink alcohol I would be loud, boisterous and noisy. This would be..."

1	2	3	4	5
Bad				Good

2.7. When I drink alcohol I would feel guilty. This would be..."

1	2	3	4	5

Bad Good

2.8. When I drink alcohol I would feel dizzy. This would be..."

1 2 3 4 5

Bad Good

2.9. When I drink alcohol I would feel moody. This would be..."

1 2 3 4 5

Bad Good

2.10. When I drink alcohol I would be clumsy. This would be..."

1 2 3 4 5

Bad Good

2.11. When I drink alcohol I would be a better lover. This would be..."

1 2 3 4 5

Bad Good

2.12. When I drink alcohol I would enjoy sex more. This would be..."

1 2 3 4 5

Bad Good

2.13. When I drink alcohol I would feel aggressive. This would be..."

1 2 3 4 5

Bad Good

2.14. When I drink alcohol I would feel peaceful. This would be..."

1 2 3 4 5

Bad Good

2.15 When I drink alcohol I would feel calm. This would be..."

1 2 3 4 5

Bad Good

Appendices 1.D Temptation and Restraint Inventory

Instructions: Please read each of the following questions carefully. Circle the number that represents your answer to each question. BE SURE TO CIRCLE ONLY ONE NUMBER FOR EACH QUESTION. Remember that your honest response -- the one that makes the most sense to you personally is the response we want. Don't worry about how other people would answer, we want your views. Please work as quickly as you can, while giving the most honest and accurate answer you can to each question. In general, your first impressions are the best.

1. When you feel anxious, are you more likely to drink?

1	2	3	4	5	6	7	8	9
Never								Always

2. When you feel lonely, are you more likely to drink?

1	2	3	4	5	6	7	8	9
Not at all								Extremely

3. How often do you attempt to cut down the amount you drink?

1	2	3	4	5	6	7	8	9
Never								Always

4. At times, do you find yourself unable to stop thinking about drinking?

1	2	3	4	5	6	7	8	9
Never								Always

5. Does seeing other people drink remind you of your efforts to control your alcohol consumption?

1	2	3	4	5	6	7	8	9
Never								Always

6. Do you ever feel so nervous that you really need a drink?

1	2	3	4	5	6	7	8	9
Never								Always

7. Do thoughts about drinking intrude into your daily activities?

1	2	3	4	5	6	7	8	9
Never								Always

8. Does seeing alcohol-related commercials, magazine ads., and/or signs for liquor stores stimulate concerns about the need to limit your drinking?

1	2	3	4	5	6	7	8	9

Never Always

9. Do you find that once you start drinking it is difficult for you to stop?

1 2 3 4 5 6 7 8 9
Never Always

10. Do feelings of guilt about drinking too much help you to control your alcohol intake?

1 2 3 4 5 6 7 8 9
Never Always

11. Is it hard to distract yourself from thinking about drinking?

1 2 3 4 5 6 7 8 9
Never Always

12. Does the sight and smell of alcohol make you think about limiting your drinking?

1 2 3 4 5 6 7 8 9
Never Always

13. How much difficulty do you have controlling your drinking?

1 2 3 4 5 6 7 8 9
None A Great Deal

14. Do you ever cut back on your drinking in an attempt to change your drinking habits?

1 2 3 4 5 6 7 8 9
Never Always

15. How much effort does it take for you to keep your drinking under control?

1 2 3 4 5 6 7 8 9
None A Great Deal

Appendices 1.E Barratt Impulsivity Scale

Directions: People differ in the ways they act and think in different situations. This is a test to measure some of the ways in which you act and think. Read each statement and place a check in the appropriate box on the right side of the page. Do not spend too much time on any statement. Answer quickly and honestly.		**Rarely/Never**	**Occasionally**	**Often**	**Almost always/ Always**
1.	I plan tasks carefully				
2.	I do things without thinking				
3.	I am happy-go-lucky				
4.	I have “racing” thoughts				
5.	I plan trips well ahead of time				
6.	I am self-controlled				
7.	I concentrate easily				
8.	I save regularly				
9.	I find it hard to sit still for long periods of time				
10.	I am a careful thinker				
11.	I plan for job security				
12.	I say things without thinking				
13.	I like to think about complex problems				
14.	I change jobs				
15.	I act “on impulse”				
16.	I get easily bored when solving thought problems				
17.	I have regular medical/dental checkups				
18.	I act on the spur of the moment				
19.	I am a steady thinker				
20.	I change where I live				
21.	I buy things on impulse				
22.	I finish what I start				
23.	I walk and move fast				
24.	I solve problems by trial-and-error				
25.	I spend or charge more than I earn				
26.	I talk fast				
27.	I have outside thoughts when thinking				
28.	I am more interested in the present than the future				
29.	I am restless at lectures or talks				
30.	I plan for the future				

Appendices 1.F Approach and Avoidance of Alcohol Questionnaire

This questionnaire relates to YOUR ATTITUDES toward alcohol RIGHT NOW. Please indicate how much you agree with the statements below by circling the number corresponding most closely to your general attitude RIGHT NOW. Your answers may range from AGREE NOT AT ALL (0) with the statement to AGREE VERY STRONGLY (8) with the statement.

		I AGREE WITH THIS STATEMENT…								
		Not At All								**Very Strongly**
1.	I would like to have a drink or two.	0	1	2	3	4	5	6	7	8
2.	I am avoiding people who are likely to offer me a drink.	0	1	2	3	4	5	6	7	8
3.	If I were in a pub or club I would want a drink.	0	1	2	3	4	5	6	7	8
4.	My desire to drink seems overwhelming.	0	1	2	3	4	5	6	7	8
5.	I am planning to drink alcohol.	0	1	2	3	4	5	6	7	8
6.	I am deliberately occupying myself so I will not drink alcohol.	0	1	2	3	4	5	6	7	8
7.	I am thinking about the benefits of being sober.	0	1	2	3	4	5	6	7	8
8.	I want to drink alcohol so much that if I start drinking now I will find it difficult to stop.	0	1	2	3	4	5	6	7	8
9.	I would accept a drink now if one was offered to me.	0	1	2	3	4	5	6	7	8
10.	I am avoiding places in which I might be tempted to drink alcohol.	0	1	2	3	4	5	6	7	8
11.	I am thinking about alcohol a lot of the time.	0	1	2	3	4	5	6	7	8
12.	I want to drink as soon as I have the chance.	0	1	2	3	4	5	6	7	8
13.	The bad things that could happen if I drink alcohol are fresh in my mind.	0	1	2	3	4	5	6	7	8
14.	If I were at a party now I would have a drink without thinking twice.	0	1	2	3	4	5	6	7	8

Appendices 1.G Brief Mood Introspection Scale

INSTRUCTIONS: Circle the response on the scale below that indicates how well each adjective or phrase describes your present mood.

1. Lively

Definitely do not feel do not feel slightly feel definitely feel

2. Drowsy

Definitely do not feel do not feel slightly feel definitely feel

3. Happy

Definitely do not feel do not feel slightly feel definitely feel

4. Grouchy

Definitely do not feel do not feel slightly feel definitely feel

5. Sad

Definitely do not feel do not feel slightly feel definitely feel

6. Peppy

Definitely do not feel do not feel slightly feel definitely feel

7. Tired

Definitely do not feel do not feel slightly feel definitely feel

8. Nervous

Definitely do not feel do not feel slightly feel definitely feel

9. Caring

Definitely do not feel do not feel slightly feel definitely feel

10. Calm

Definitely do not feel do not feel slightly feel definitely feel

11. Content

Definitely do not feel do not feel slightly feel definitely feel

12. Loving

Definitely do not feel do not feel slightly feel definitely feel

13. Gloomy

Definitely do not feel do not feel slightly feel definitely feel

14. Fed up

Definitely do not feel do not feel slightly feel definitely feel

15. Jittery

Definitely do not feel do not feel slightly feel definitely feel

16. Active

Appendices 1.H Subjective Intoxication Scale

This questionnaire is concerned with how you feel *right now*.
Please place a mark on each line to indicate how you feel on each dimension.

Light headed

Not at all Slightly Moderately Quite a lot Extremely

Irritable

Not at all Slightly Moderately Quite a lot Extremely

Stimulated

Not at all Slightly Moderately Quite a lot Extremely

Alert

Not at all Slightly Moderately Quite a lot Extremely

Relaxed

Not at all Slightly Moderately Quite a lot Extremely

Contented

Not at all Slightly Moderately Quite a lot Extremely

Appendices 1.I *Ad Libitum* Taste Test

Please consume as much as you like DRINK 1 in order to give an answer for the questions below. You can take as long as necessary.

How fruity was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How smooth was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How sweet was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How refreshing was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How bitter was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How strong tasting was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How gassy was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How pleasant was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How light was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How tasty was DRINK 1?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all

Please consume as much as you like DRINK 2 in order to give an answer for the questions below. You can take as long as necessary.

How fruity was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How smooth was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How sweet was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How refreshing was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How bitter was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How strong tasting was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How gassy was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How pleasant was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How light was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all 10= Extremely.

How tasty was DRINK 2?
0 1 2 3 4 5 6 7 8 9 10
0= Not at all

Appendices 1.J Alcohol Sensitivity Questionnaire

<u>Please circle YES or NO for each question and answer the questions below each time you have answered YES.</u>

1. Do you ever experience a hangover after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without experiencing a hangover after drinking alcohol?

……

2. Do you ever pass out after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without passing out after drinking alcohol?

……

3. Do you ever throw up (vomit) after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without vomiting after drinking alcohol?

……

4. Do you ever feel nauseated after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without feeling nauseated after drinking alcohol?

……

5. Do you ever forget part of an evening (i.e. blackoouts) after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without forgetting part of an evening after drinking alcohol?

……

6. Do you ever feel dizzy or feel things spinning after drinking alcohol?

YES or NO

IF YES, what is the maximum number of drinks you could consume without feeling dizzy after drinking alcohol?

……

7. Do you ever become more talkative after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before becoming more talkative after drinking alcohol?

……

8. Do you ever become more flirtatious after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before becoming more flirtatious after drinking alcohol?

……

9. Do you ever feel high or “buzzed” after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling high or buzzed after drinking alcohol?

……

10. Do you ever feel more socially at ease after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling more socially at ease after drinking alcohol?

……

11. Do you ever feel more relaxed after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling more relaxed after drinking alcohol?

……

12. Do you ever feel sluggish after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling sluggish after drinking alcohol?

……

13. Do you ever feel less inhibited after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling less inhibited after drinking alcohol?

……

14. Do you ever feel that your driving would be affected after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling your driving would be affected after drinking alcohol?

……

15. Do you ever feel sedated or sleepy after drinking alcohol?

YES or NO

IF YES, what is the minimum number of drinks you could consume before feeling sedated or sleepy after drinking alcohol?

……

Appendices 1.K State Trait Anxiety Inventory

State Items

DIRECTIONS:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel *right* now, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I feel strained	1	2	3	4
5. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am presently worrying over possible misfortunes	1	2	3	4
8. I feel satisfied	1	2	3	4
9. I feel frightened	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel indecisive	1	2	3	4
15. I am relaxed	1	2	3	4
16. I feel content	1	2	3	4
17. I am worried	1	2	3	4
18. I feel confused	1	2	3	4
19. I feel steady	1	2	3	4
20. I feel pleasant	1	2	3	4

STAIP-AD Test Form Y
www.mindgarden.com

SELF-EVALUATION QUESTIONNAIRE

STAI Form Y-2

Name_____Date_____

DIRECTIONS

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you *generally* feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
21. I feel pleasant	1	2	3	4
22. I feel nervous and restless	1	2	3	4
23. I feel satisfied with myself	1	2	3	4
24. I wish I could be as happy as others seem to be	1	2	3	4
25. I feel like a failure	1	2	3	4
26. I feel rested	1	2	3	4
27. I am "calm, cool, and collected"	1	2	3	4
28. I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
29. I worry too much over something that really doesn't matter	1	2	3	4
30. I am happy	1	2	3	4
31. I have disturbing thoughts	1	2	3	4
32. I lack self-confidence	1	2	3	4
33. I feel secure	1	2	3	4
34. I make decisions easily	1	2	3	4
35. I feel inadequate	1	2	3	4
36. I am content	1	2	3	4
37. Some unimportant thought runs through my mind and bothers me	1	2	3	4
38. I take disappointments so keenly that I can't put them out of my mind	1	2	3	4
39. I am a steady person	1	2	3	4
40. I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

STAIP-AD Test Form Y
www.mindgarden.com

Appendices 1.L Funnelled Debrief (studies one-three)

1. What was the purpose of this experiment?

2 . The computer task was designed to…….

Measure reaction times in response to the target stimuli [ ]

Assess my cognitive processing [ ]

Train me to think more quickly [ ]

Measure reaction times to correlate with alcohol use [ ]

Assess my behavioural impulsivity (response inhibition) [ ]

I do not know the purpose [ ]

3. The purpose of this taste test was to…….

Measure my liking for each drink [ ]

Measure my preference for each drink [ ]

Measure my preferences to each drink in response to the computer task [ ]

Measure how much I drank in response to the computer task [ ]

Find out which drink I preferred [ ]

Measure whether I would drink less/more beer in response to my answers on the questionnaire [ ]

I do not know the purpose [ ]

Appendices 1.M Funnelled Debrief (Study six)

2. What was the purpose of this experiment?

2 . The computer task was designed to…….

Measure reaction times in response to the target stimuli [ ]

Assess my cognitive processing [ ]

Train me to think more quickly [ ]

Measure reaction times to correlate with alcohol use [ ]

Assess my behavioural impulsivity (response inhibition) [ ]

I do not know the purpose [ ]

4. The purpose of this taste test was to…….

Measure my liking for each drink [ ]

Measure my preference for each drink [ ]

Measure my preferences to each drink in response to the computer task [ ]

Measure how much I drank in response to the computer task [ ]

Find out which drink I preferred [ ]

Measure whether I would drink less/more beer in response to my answers on the questionnaire [ ]

I do not know the purpose [ ]

1. The purpose of the 5 min presentation task was to…….

Measure my organisation, articulation, openness & defensiveness [ ]

To measure my ability to think on the spot and perform under pressure [ ]

To induce stress [ ]

To assess my personality [ ]

To investigate if I would increase/decrease alcohol consumption in response to this [ ]

To see if my performance on the computer tasks was affected [ ]

I do not know the purpose [ ]

Appendices 2 Pre-registration of the effect of alcohol cues on proactive inhibitory control and signal detection.

Laura Baines Paul Christiansen Matt Field Andrew Jones

Introduction

Inhibitory control is defined as the inability to suppress, postpone or alter a response that is no longer necessary or is inappropriate given the current situation (Jones & Field, 2015; Logan et al, 1984). This ability has substantial overlap with self-control (Baumeister, 2014) and as a result is implicated in theoretical models of addiction (de Wit, 2009; Goldstein & Volkow, 2011). Experimental research supports theoretical predictions, with meta-analyses demonstrating that inhibitory control is impaired in heavy drinkers / alcoholics compared to controls (Smith et al., 2014), and associations with hazardous drinking are often reported in laboratory studies (Christiansen et al., 2012; Houston et al., 2014).

These models however present an over-simplistic view of inhibitory control as a reactive stopping response, whilst failing to recognise the complexity of the behaviour. A recent cognitive model (Verbruggen et al., 2014) has argued that inhibitory control involves a combination of sequential processes including: signal detection (identifying an inhibitory signal), followed by selecting and executing (or inhibiting) an appropriate action. Additionally, the model suggests that each sub-process is underpinned by other non-inhibitory processes, for example, proactive control and associative learning, both of which may play a significant role in substance misuse.

In terms of associative learning, alcohol-related cues are thought to promote an associative approach response (Field et al., 2011; Field et al., 2008). Due to rapid automatic approach behaviour, the exposure to alcohol-related cues is thought to impair inhibitory control (Jones et al., 2013). Indeed laboratory evidence supports this, with alcohol cues embedded into Stop Signal and Go/No-Go tasks causing temporary impairments in inhibition (Jones & Field, 2015; Petit et al., 2012). Despite this, it is unclear whether the impairing effects of alcohol cues on inhibitory control arise from effects on proactive control, reactive control or signal detection (or a combination of these). Alcohol cues may compete with inhibitory signals in the environment for attentional selection (Pessoa et al., 2012) reducing the detection of inhibitory signals, and may induce cognitive biases that effect the maintenance of proactive control and the execution of a reactive stopping response (Stacy &

Wiers, 2010). Therefore, it is likely that both signal detection and proactive control are influenced by alcohol-related cues and contexts.

As such, the aim of this study is to investigate whether alcohol cues and contexts impair inhibitory sub-processes and proactive control and whether these deficits are related to individual differences in alcohol consumption. Participants will complete a modified stop signal task based on Verbruggen et al (Verbruggen et al., 2014) under alcohol cue-exposure and a control condition. Study hypotheses are stated below:

Hypothesis 1: Craving will be increased following alcohol cue-exposure, compared to neutral cue exposure.

Hypothesis 2: Heavy drinkers will show deficits in i) proactive control, ii) signal-detection and iii) reactive control, following exposure to alcohol-related cues.

Hypothesis 3: Participants will consume more beer (as a % of total fluid consumed), following exposure to alcohol-related cues.

Hypothesis 4: Proactive control and signal detection deficits will predict unique variance in alcohol consumption and related problems, after controlling for reactive inhibition.

Hypothesis *5*: The effects of alcohol cues on ad libitum alcohol consumption will be partially mediated by changes in the different components of control.

Methods

Participants

Heavy drinkers (N=64) will take part in a laboratory study with two sessions, approximately one week apart. We conducted a power analyses based on a pooled effect size (d = .39, α = .05, $1\text{-}\beta$ = 90%) from studies which have examined the effect of alcohol-related cues on inhibitory control in heavy drinkers (Czapla et al., 2015; Jones & Field, 2015; Kreusch et al., 2013). Heavy drinking will be defined using UK government guidelines: males and females who consume > 14 UK units of alcohol per week (1 UK unit = 8g of pure alcohol). Participants will be eligible to participate if they are aged 18 or over, a fluent English speaker and report a motivation to reduce their alcohol consumption. Exclusion criteria will include a self-reported current or previous diagnosis of substance use disorder, ADHD, psychiatric disorder, a current/recent illness (e.g. flu) that could increase sensitivity to alcohol, or taking medications (e.g. antidepressants) that are affected by alcohol. Finally, participants cannot take part if they have an allergy to beer or fruit juice, are currently pregnant or breastfeeding. The study has been approved by the University of Liverpool's Institutional Review Board.

Materials

Questionnaires

The Timeline follow back (Sobell & Sobell, 1990) will be administered to measure retrospective alcohol consumption in units (one UK unit = 8 g of alcohol), over the previous two weeks. A guide providing the number of units in standard UK drinks will be provided to assist participants in calculating their alcohol consumption. *The Alcohol use disorders identification test (Saunders et al., 1993)* will be administered to measure hazardous drinking. This includes 10 fixed-response items and scores are measured between 0 and 40. Higher scores are indicative of greater alcohol consumption, with a score over 8 indicative of hazardous drinking. *The Brief comprehensive effects of alcohol questionnaire (Ham et al., 2005)* contains 15 items to measure alcohol outcome expectancies (what participants expect to happen when they consume alcohol). *The Temptation Restraint Inventory (Collins & Lapp, 1992)* to measure drinking restraint (preoccupation with and efforts to reduce drinking). This consists of 15 items and gives scores on two sub-scales; Cognitive behavioural control (CBC) and Cognitive emotion preoccupation (CEP). *Barratt Impulsivity Scale (Patton et al., 1995)* to measure impulsivity across three dimensions (motor, non-planning and attentional). This consists of 30 items with higher scores indicating increased impulsivity. *The Approach and Avoidance of Alcohol Questionnaire (McEvoy et al., 2004)* to measure self-reported craving. This consists of 14 items scored from 0 (not at all) to 8 (very strong) measuring three sub-scales of craving; mild inclinations to drink, intense inclinations to drink and inclinations to avoid alcohol. Participants will also complete a short questionnaire to measure awareness of the experimental aims of the study. This will include an open question asking what the purpose of the experiment was and two fixed-response questions asking the purpose of the computer task and the taste test (see supplementary material 1).

Modified Stop-Signal task (SST: Verbruggen et al., 2014))

Participants will complete a modified Stop-Signal task, which isolates proactive control, reactive control and signal detection. At the beginning of each trial a white fixation line will appear in the middle of the screen for 500ms, as well as a white border around the edge of the screen display. Following these, two words will appear, one immediately above the line and one immediately below the fixation line. These words will be natural-related (e.g. lion) or man-made (e.g. desk). Natural words are target words and participants have to respond as quickly as possible to their position in relation to the line (above or below) by a key press. Man-made words are distractors. Depending on condition, the neutral-related image or

alcohol related image appeared in the background on each trial. The task consists of three blocks, which are presented in a randomised, counterbalanced order:

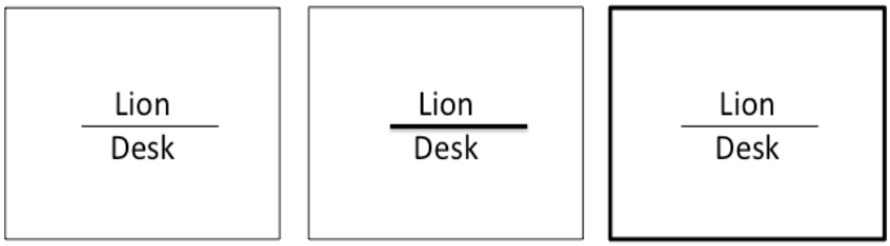
No-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 100% of trials (128 in total).

Central-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 75% of trials (96 in total). On the remaining 25% (32 in total) trials, the white fixation line between the words increased in size by 300%. Participants are told to try and withhold their response to the target word position if this happens.

Peripheral-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 75% of trials (96 in total). On the remaining 25% (32 in total) trials, the white square around the edge of the display increased in size by 300%. Participants are told to try and withhold their response to the target word position if this happens.

In both the central-signal and peripheral signal block the delay between presentation of the target and distractor word and the colour change of the stop signals (fixation line or square around the display) was adjusted on a trial-by-trial basis using a tracking procedure (Verbruggen & Logan, 2009). In each both the initial delay was 250 ms, if participants failed to inhibit the delay decreased by 50 ms making subsequent inhibition easier, if participants successfully inhibited then the delay increased by 50 ms making subsequent inhibition more difficult. Proactive control is inferred from the degree of reaction time slowing on stop-signal blocks compared to no-signal blocks (this indicates motivation to inhibit on the stop-signal blocks). Signal detection is inferred from the difference in stop signal reaction time (SSRT) between central-signal and periphery-signal blocks. Reactive control is inferred as the mean SSRT collapsed across central and peripheral signal blocks. Effects of alcohol-cues on each process will be measured by comparing performance across conditions (alcohol context, neutral context).

Fig 1 Schematic of the modified Stop-signal task



No-signal trial | Central stop-signal trial | Periphery stop-signal trial

'In this task your target words are Natural objects. Press the Y KEY if the natural word appears above the fixation line. Press the N KEY if the natural word appears below the line. Your distractor words are man-made objects. Do not respond to these. If you see the fixation line or the box around the words become thicker, you should try to WITHOLD your response.'

Alcohol background scenes will be incorporated into the task in alcohol cue-exposure session

Neutral background scenes will be incorporated into the task in neutral cue-exposure session

***Ad libitum* taste test**

Participants will receive 250ml of chilled Skol beer (2.8% vol. ABV) and 250ml of chilled fresh orange juice (non-alcoholic beverage). They will not be informed of the brands used and will be given each drink simultaneously in unmarked glasses. Participants will be asked to taste and rate the drinks on various gustatory dimensions e.g. bitter, gassy using visual analogue scales and will be told to 'drink as much or as little as you like in order to make accurate judgements'. This task or slight variations thereof has good construct validity (Jones et al., 2015). Participants will be told they have 10 minutes to complete the taste test, however, they will also be told that alcohol will impair performance on the next task, in which they will have the opportunity to win small amounts of money (Christiansen et al., 2012), in order to increase their motivation to reduce their intake. The volume of each drink consumed will be recorded unobtrusively at the end of each session. We will then calculate the amount of beer as a percentage of total fluid consumed.

Balloon Analogue Risk Task (BART: (Lejuez et al., 2003))

Participants will complete a short cognitive task in which they have to click a mouse to pump up simulated balloons (see schematic). They will be presented with one balloon per trial and will complete 10 trials. Each time participants click to pump up the balloon, the balloon will increase in size and they will hypothetically collect $0.05 in a temporary bank. They can transfer this money to a "permanent" bank by clicking collect. However, they will be informed that if the balloon bursts, they will lose the money in the temporary bank. Once the balloon has burst or the participant has collected the money, the size of the balloon will be reset and the temporary bank will be reset to $0. We will set the balloons to burst on a variable ratio, with 64 pumps as the average explosion point. We include this task to increase participants' belief that they need to restrict their alcohol consumption during the taste-test to perform well on this task, across both conditions. Performance on this task is of secondary importance here. However, we will calculate 'Adjusted average pumps' (which represents the mean number of pumps on balloons which did not burst), as the outcome variable based on previous research (e.g. (Lejeuz et al., 2003)).

Procedure/Design

Participants will attend two sessions approximately week apart, the order of which will be counterbalanced. One session will be completed in a standard neutral laboratory, the other will be completed in the University of Liverpool's Bar Laboratory (https://www.liverpool.ac.uk/psychology-health-and-society/facilities/bar-lab/), which is fitted like a typical UK bar and contains advertisements for alcohol, beer pumps etc. Participants will be breathalysed at the beginning of each session and must have a BAC of 0.0mg/l in order to take part. Participants will first complete demographics, the battery of questionnaires measuring alcohol use and personality (first session only) and the AAQ to measure craving before the SST. They will then complete the three blocks of the Stop-signal task with the appropriate background depending on session. Before each block of the task, participants will be asked to smell a drink and allow a small amount to touch their lips (beer in the alcohol session, water in the neutral session), to increase cue-reactivity further. Next, participants will fill in the AAAQ to measure craving following the task. They will then complete the ad libitum taste and will be informed that alcohol may impair their performance on the last task, in which they have the opportunity to win small amounts of money. Lastly participants will complete the BART task and a final breath alcohol sample. At the end of the

final session, participants will also complete a short questionnaire assessing their awareness of experimental aims (see supplementary materials 1).

Proposed Analyses

Hypothesis 1: ***Craving will be increased following alcohol cue-exposure, compared to neutral cue exposure.***

To examine whether alcohol cue exposure increases craving, scores on the AAAQ will be analysed using a 3 (subscale: inclined/indulgent, obsessed/compelled, resolved-regulated) x 2 (time: pre-manipulation, post-manipulation) x 2 (condition: alcohol cue exposure, control / neutral) repeated measures ANOVA. Main effects and interactions will be investigated using the appropriate comparisons.

Hypothesis 2: ***Heavy drinkers will show deficits in i) proactive control, ii) signal-detection and iii) reactive control, following exposure to alcohol-related cues.***

Deficits in proactive control will be analysed using a 2 (block: no-signal block, central and peripheral signal blocks) x 2 (condition: alcohol cue exposure, control / neutral) repeated measures ANOVA on reaction times. Main effects and interactions will be investigated using the appropriate comparisons. Deficits in signal-detection and reactive control will be analysed using a 2 (block: central signal, peripheral signal) x 2 (condition: alcohol cue exposure, control / neutral) repeated measures ANOVA on SSRT. Main effects and interactions will be investigated using the appropriate comparisons.

Hypothesis 3: ***Participants will consume more beer (as a % of total fluid consumed) in the alcohol session than neutral session.***

To examine differences in *ad-libitum* alcohol consumption we will conduct independent t-tests on beer consumed (as a percentage of total fluid) .

Hypothesis 4: ***Proactive control and signal detection deficits will predict unique variance in alcohol consumption and related problems, after controlling for reactive inhibition.***

To examine whether indices of inhibitory control we will run multiple regression analyses to investigate if proactive control, signal detection and reactive control predict unique variance in beer (as % of total fluid consumed). These analyses will be run separately by condition.

Hypothesis ***5: The effects of alcohol cues on ad libitum alcohol consumption will be partially mediated by changes in the different components of control.***

To examine whether changes in the different components of control partially mediate the effect of alcohol cues on ad libitum alcohol consumption, we will run a within-subjects mediation analysis using MEMORE macro for SPSS (Montoya & Hayes, 2016). This will estimate the total, direct and indirect effects of alcohol cues on ad libitum alcohol consumption through changes in the different components of control (reactive control, proactive control and signal detection).

Exploratory analyses

Any exploratory analyses will be labelled as such in the publication of the data**.**

Appendices 3 Pre-registration of the effect of acute alcohol intoxication on reactive and proactive control, and signal detection

Laura Baines Paul Christiansen Matt Field Andrew Jones

Introduction

Inhibitory control is defined as a the inability to suppress, postpone or alter a response that is no longer necessary or is inappropriate given the current situation (Jones & Field, 2015; Logan et al, 1984). This ability has substantial overlap with self-control (Baumeister, 2014) and as a result is implicated in theoretical models of addiction (de Wit, 2009; Goldstein & Volkow, 2011). Poor inhibitory control has been associated with hazardous drinking in numerous laboratory studies (Christiansen et al., 2012; Houston et al., 2014) and experimental research has demonstrated that alcohol impairs inhibitory control at doses that would not lead to global deficits in cognitive performance (Field et al., 2010). Furthermore, research suggests the magnitude of inhibitory deficits following alcohol intoxication is associated with *ad-libitum* consumption when sober (Weafer & Fillmore, 2008).

Despite this, theoretical models present an over-simplistic view of inhibitory control as a reactive stopping response, whilst failing to recognise the underlying and complex mechanistic nature of inhibitory control. A recent cognitive model (Verbruggen et al., 2014) has argued that inhibitory control involves a combination of sequential processes including: signal detection (identifying an inhibitory signal), followed by selecting and executing an appropriate action. Additionally, each sub-process is underpinned by other non-inhibitory processes, including proactive control and associative learning, both of which may play a significant role in substance addiction.

Consequently, although research has shown that inhibitory control is compromised by moderate doses of alcohol (e.g. (Abroms & Fillmore, 2004; de Wit et al., 2000; Marczinski et al., 2005)) and that these doses increase both objective (e.g. *ad libitum* consumption) and subjective (e.g. craving) measures of alcohol seeking (e.g. Christiansen et al., 2012; Fernie et al., 2012; Rose & Grunsell, 2008)), it is

unclear whether impairments in inhibitory control arise from the effects of alcohol on proactive control, reactive control or signal detection (or a combination).

Further research has demonstrated that an alcohol-placebo prime impairs inhibitory control (Christiansen et al., 2016) and increases craving and *ad libitum* consumption (e.g. (Christiansen et al., 2013; Rose et al., 2013)). Specifically, Christiansen et al (Christiansen et al., 2016) also showed that Go/No-Go task performance correlated with expectancies of behavioural and cognitive impairment following placebo-alcohol. Furthermore, Leeman et al (Leeman et al, 2009) showed that *ad-libitum* consumption was predicted by craving following a placebo-alcohol drink, but not an alcohol drink. These imply that the anticipated effects of alcohol play may at least some role in inhibitory control deficits and increased alcohol seeking following the consumption of an alcohol prime. Despite this, there is an absence of empirical research investigating the effects of placebo-alcohol directly on inhibitory control and therefore it is unclear whether any impairment in inhibitory control from the anticipated effects of alcohol arises from impairment in proactive, reactive control or signal detection.

Therefore, the aim of the study is to investigate whether both a priming dose of alcohol and the anticipated effects of alcohol impair inhibitory sub-processes and proactive control, compared to a control condition, and whether these are related to individual difference in alcohol consumption. The inclusion of a placebo-alcohol and control condition will allow us to disentangle the pharmacological from the anticipatory effects of alcohol-intoxication. Study hypotheses are stated below:

Hypothesis 1: Priming participants with alcohol will increase subjective intoxication ratings and motivation to drink (measured by an estimation of units in the priming drink, mean BAC; (post-drink, end of session), scores on subjective intoxication scales and self-reported craving), compared to placebo-alcohol and control conditions. We also hypothesise that increases in subjective intoxication ratings and motivation to drink will be observed in the placebo-alcohol condition compared to control.

Hypothesis 2: Alcohol intoxication will cause deficits in i) proactive control, ii) signal detection and iii) reactive control, compared to the placebo-alcohol and control priming drinks (placebo-alcohol will also induce greater impairments than control, but not to the same extent as alcohol).

Hypothesis 3: Participants will consume more beer (as a % of total fluid) following alcohol compared to placebo-alcohol and controls (placebo-alcohol will induce greater consumption compared to control condition, but not to the same extent as alcohol).

Hypothesis 4*:* Following alcohol intoxication, proactive control, signal detection and reactive control will predict unique variance in alcohol consumption.

Hypothesis 5: The effects of alcohol intoxication on ad libitum alcohol consumption will be partially mediated by changes in the different components of control .

Methods

Participants

Heavy drinkers (N = 36) will take part in a laboratory study with three sessions, approximately one week apart. The number of participants was decided upon using a power calculation to find a medium effect size (d = .50) at α = .05, and 90% power. Studies have demonstrated larger effect sizes of alcohol impairments on inhibitory control (Stroop) tasks (e.g. Christiansen et al, 2016, d =. 61) however as no research has examined the effects on inhibitory subcomponents we opted for a more conservative estimate of d = .50. Heavy drinking will be defined using UK government guidelines: males and females who consume > 14 UK units of alcohol per week (1 UK unit = 8g of pure alcohol). Other inclusion criteria will include being aged 18 or over, and a fluent English speaker, self-reported motivation to reduce their alcohol consumption. We aim to recruit equal number of males and females. Exclusion criteria will include a self-reported current or previous diagnosis of substance use disorder, ADHD, psychiatric disorder, a current/recent illness (e.g. flu) that could increase sensitivity to alcohol, or taking medication (e.g. antidepressants) that are affected by alcohol. Finally, participants cannot take part if they have an allergy to beer or fruit juice, or are currently pregnant or breastfeeding.

Materials

Drink preparation

The alcoholic drink will contain vodka (Smirnoff Red, 37.5% alcohol by volume (ABV)) and chilled tonic water. The alcohol dose will be calculated as 0.6g of pure alcohol per kg of body weight (maximum 200ml) and the drink mixed one part vodka,

three parts tonic. The placebo-alcohol drink will contain chilled tonic water, the total volume of which will be the same as the alcoholic drink. Vodka mist will be sprayed on the surface of the drink and smeared onto the rim of the glass. Tabasco sauce will also be added to simulate the taste of alcohol. The control drink will consist of chilled water; the total volume of this will be identical to the alcoholic and placebo drink.

Questionnaires

The Timeline follow back (Sobell & Sobeel, 1990), will be administered to measure retrospective alcohol consumption in units (one UK unit = 8 g of alcohol), over the previous two weeks. A guide providing the number of units in standard UK drinks will be provided to assist participants in calculating their alcohol consumption. *The Alcohol use disorders identification test (Saunders et al, 1993)* will be administered to measure hazardous drinking. This includes 10 fixed-response items and scores are measured between 0 and 40. Higher scores are indicative of greater alcohol consumption, with a score over 8 indicative of hazardous drinking. *The Brief comprehensive effects of alcohol questionnaire (Ham et al, 2005)* contains 15 items to measure alcohol outcome expectancies (what participants expect to happen when they consume alcohol). *The Temptation Restraint Inventory (Collins & Lapp, 1992)* to measure drinking restraint (preoccupation with and efforts to reduce drinking). This consists of 15 items and gives scores on two sub-scales; Cognitive behavioural control (CBC) and Cognitive emotion preoccupation (CEP). *Barratt Impulsivity Scale (Patton et al, 1995)* to measure impulsivity across three dimensions (motor, non-planning and attentional). This consists of 30 items with higher scores indicating increased impulsivity. *The Approach and Avoidance of Alcohol Questionnaire (McEvoy et al, 2004)* to measure self-reported craving. This consists of 14 items scored from 0 (not at all) to 8 (very strong) measuring three sub-scales of craving; mild inclinations to drink, intense inclinations to drink and inclinations to avoid alcohol. *The Subjective intoxication scales (SIS: Duka et al, 1998))* to measure subjective feelings of 'lightheaded,' 'irritable', 'stimulated', 'alert', 'relaxed' and 'contented' on six scales from 'Not at all' to 'Extremely. Participants will also complete a short questionnaire to measure awareness of the experimental aims of the study. This will include an open question asking what the purpose of the experiment was and two fixed-response questions asking the purpose of the computer task and the taste test (see supplementary material 1).

Stop-signal task (SST; Verbruggen et al, 2014))

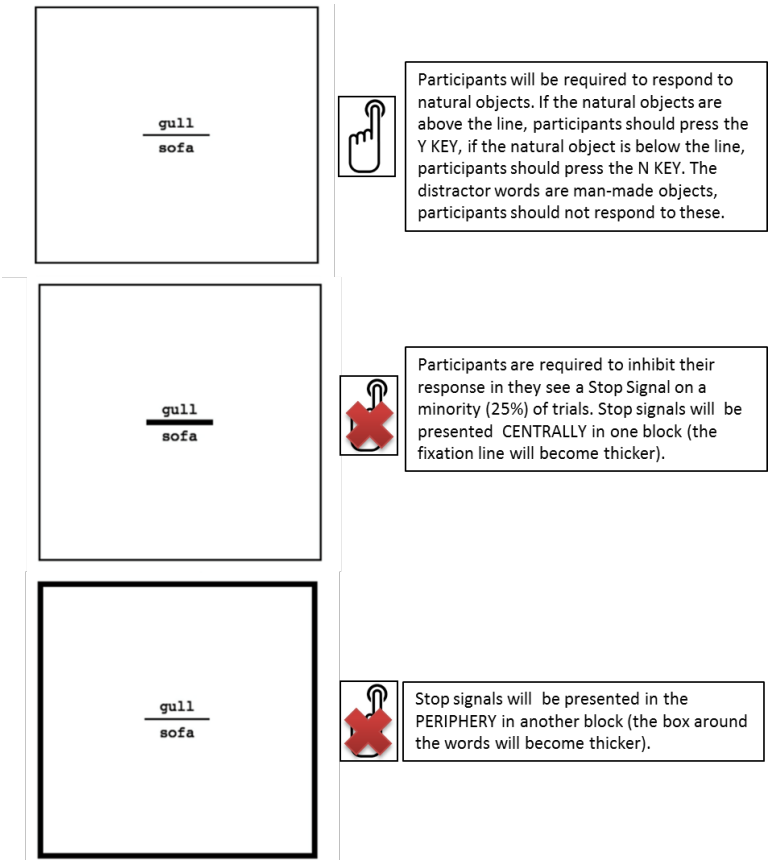
Participants will complete a modified Stop-Signal task, which isolates proactive control, reactive control and signal detection. At the beginning of each trial a white fixation line will appear in the middle of the screen for 500ms, as well as a white border around the edge of the screen display. Two words will then appear, one immediately above the line and one immediately below. These words will be natural-related (e.g. lion) or man-made (e.g. desk). Natural words are target words and participants have to respond as quickly as possible to their position in relation to the line (above or below) by a key press. Man-made words are distractors. The task consists of three blocks, which were presented in a randomised, counterbalanced order:

No-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 100% of trials (128 in total).

Central-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 75% of trials (96 in total). On the remaining 25% (32 in total) trials, the white fixation line between the words increased in size by 300%. Participants are told to try and withhold their response to the target word position if this happens.

Peripheral-signal block: In this block participants identify the position of the target word in relation to the line without interruption on 75% of trials (96 in total). On the remaining 25% (32 in total) trials, the white square around the edge of the display increased in size by 300%. Participants are told to try and withhold their response to the target word position if this happens. In both the central-signal and peripheral signal block the delay between presentation of the target and distractor word and the colour change of the stop signals (fixation line or square around the display) was adjusted on a trial-by-trial basis using a tracking procedure (Verbruggen & Logan, 2009) In each both the initial delay was 250 ms, if participants failed to inhibit the delay decreased by 50 ms making subsequent inhibition easier, if participants successfully inhibited then the delay increased by 50 ms making subsequent inhibition more difficult.

Fig 1 Schematic of the modified Stop-signal task



Proactive control is inferred from the degree of reaction time slowing on stop-signal blocks compared to no-signal blocks (this indicates motivation to inhibit on the stop-signal blocks). Signal detection is inferred from the difference in stop signal reaction time (SSRT) between central-signal and periphery-signal blocks. Reactive control is inferred as the mean SSRT collapsed across central and peripheral signal blocks. Effects of alcohol-cues on each process will be measured by comparing performance across conditions (alcohol, alcohol-placebo, control).

Ad libitum taste test

Participants will receive 250ml of chilled Skol beer (2.8% vol. ABV) and 250ml of chilled fresh orange juice (non-alcoholic beverage). They will not be informed of the brands used and will be given each drink simultaneously in unmarked glasses. Participants will be asked to taste and rate the drinks on various gustatory dimensions e.g. bitter, gassy using visual analogue scales and will be told to 'drink as much or as little as you like in order to make accurate judgements'. This task or slight variations

thereof has good construct validity (Jones et al, 2015). Participants will be told they have 10 minutes to complete the taste test, however, they will also be told that alcohol will impair performance on the next task, in which they will have the opportunity to win small amounts of money (Christiansen et al., 2012) in order to increase their motivation to reduce their intake. The volume of each drink consumed will be recorded at the end of each session. We will then calculate the amount of beer as a percentage of total fluid consumed for each session.

Balloon Analogue Risk Task (BART; Lejeuz et al, 2003))

Participants will complete a short cognitive task in which they have to click a mouse to pump up simulated balloons (see schematic). They will be presented with one balloon per trial and will complete 10 trials. Each time participants click to pump up the balloon, the balloon will increase in size and they will hypothetically collect $0.05 in a temporary bank. They can transfer this money to a "permanent" bank by clicking collect. However, they will be informed that if the balloon bursts, they will lose the money in the temporary bank. Once the balloon has burst or the participant has collected the money, the size of the balloon will be reset and the temporary bank will be reset to $0. We will set the balloons to burst on a variable ratio, with 64 Pumps as the average explosion point. We include this task to increase participants' belief that they need to restrict their alcohol consumption during the taste-test to perform well on this task, across both conditions. Performance on this task is of secondary importance here. However, we will calculate 'Adjusted average pumps' (which represents the mean number of pumps on balloons which did not burst), as the outcome variable based on previous research (e.g. Lejeuz et al, 2003)).

Procedure/Design

Participants will attend three sessions (alcohol, alcohol-placebo and control) in a neutral laboratory. Each session will have to be at least one week apart and will be completed in a pseudo-counterbalanced order, meaning all participants will complete the control session first, followed by either the placebo or alcohol session in a counterbalanced order. Participants will be informed that the experiment is investigating the effect of a high, low and no dose of alcohol on taste perception. Participants will be breathalysed at the beginning of each session and must have a BAC of 0.0mg/l in order to take part. Participants will first complete demographics

and a battery of questionnaires measuring personality and alcohol use (first session only). They will then complete the AAAQ and dependent on condition, will receive either the alcohol, placebo or control drink (in 2 glasses) and will be asked to consume this within 10 minutes. This will be followed by a 20-minute absorption period. Participants will then complete the AAAQ, SIS and a breath alcohol sample, followed by the stop-signal task. Following the task, participants will complete the *ad-libitum* taste and will be informed that alcohol may impair their performance on the last task, in which they have the opportunity to win small amounts of money. Lastly participants will complete the BART task and a final breath alcohol sample. They will be informed at the beginning of the study that if their BAC is greater than 0.17mg/l, they will be asked to stay in the laboratory until it reaches this level or below. If they wish to leave, they will be asked to sign a waiver form ensuring they are aware that they must not drive, ride a bike, operate machinery, or exercise for at least 4-5 hours. At the end of the final session, participants will also complete a short questionnaire assessing their awareness of experimental aims (see supplementary materials one).

Proposed Analyses

Hypothesis 1*: Priming participants with alcohol will increase subjective intoxication ratings and motivation to drink (measured by an estimation of units in the priming drink, mean BAC; (post-drink, end of session), scores on subjective intoxication scales and self-reported craving), compared to placebo-alcohol and control conditions. Increases in subjective intoxication ratings and motivation to drink will be observed in the placebo-alcohol condition compared to control.*

To examine differences in the estimated number of alcohol units in the priming drink and scores on the SIS in each session, three-way repeated measures ANOVAs will be conducted (alcohol, alcohol-placebo, control). To examine differences in mean BAC between post-drink assessment and the end of the sessions, a 3 (session: alcohol, alcohol-placebo, control) x 2 (time: post-drink assessment, end of session) repeated measures ANOVA will be conducted. Finally to examine whether alcohol increases craving, scores on the AAAQ will be analysed using a 3 (subscale: inclined/indulgent, obsessed/compelled, resolved-regulated) x 2 (time: pre-drink, post-drink) x 3 (condition: alcohol, placebo, control) repeated measures ANOVA. Main effects and interactions will be investigated using the appropriate comparisons.

Hypothesis 2: ***Alcohol intoxication will cause deficits in i) proactive control, ii) signal detection and iii) reactive control, compared to the placebo-alcohol and control priming drinks (placebo-alcohol will also induce greater impairments than control, but not to the same extent as alcohol).***

Deficits in proactive control will be analysed using a 2 (block: no-signal block, central and peripheral signal blocks) x 3 (condition: alcohol, alcohol-placebo, control) repeated measures ANOVA on reaction times. Main effects and interactions will be investigated using the appropriate comparisons. Deficits in signal detection and reactive control will be analysed using a 2 (block: central signal, peripheral signal) x 3 (condition: alcohol, placebo-alcohol, control) repeated measures ANOVA on SSRT. Main effects and interactions will be investigated using the appropriate comparisons.

Hypothesis 3: ***Participants will consume more beer (as a % of total fluid) following alcohol compared to placebo-alcohol and controls (placebo-alcohol will induce greater consumption compared to control condition, but not to the same extent as alcohol).***

To examine differences in *ad-libitum* alcohol consumption (beer as a % of total fluid consumed) we will conduct a repeated measures ANOVA (condition: alcohol, placebo-alcohol, control). We will also investigate differences in ratings of pleasantness between sessions using repeated measures ANOVA, similar to above.

Hypothesis 4*: Following alcohol intoxication, proactive control, signal detection and reactive control will predict unique variance in alcohol consumption.*

We will run multiple regression analyses separately across each condition to investigate if indices of inhibitory control (proactive, reactive control and signal detection) predict unique variance in beer (as % of total fluid consumed) in the *ad libitum* taste test.

Hypothesis ***5: The effects of alcohol intoxication on ad libitum alcohol consumption will be partially mediated by changes in the different components of control.***

To examine whether changes in the different components of control partially mediate the effect of alcohol intoxication on ad libitum alcohol consumption, we will run a

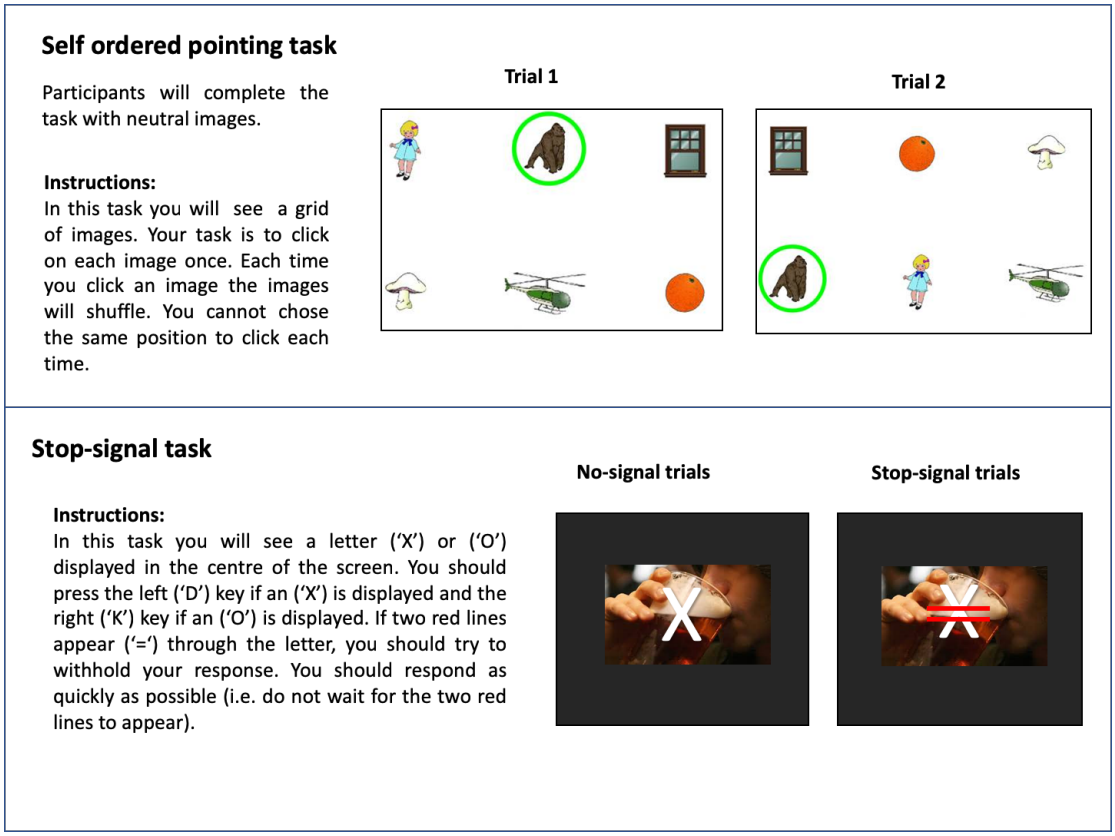
within-subjects mediation analysis using MEMORE macro for SPSS (Montoya & Hayes, 2016). This will estimate the total, direct and indirect effects of alcohol intoxication on ad libitum alcohol consumption through changes in the different components of control (reactive control, proactive control and signal detection).

Exploratory analyses

We also plan to conduct exploratory analyses, for example, exploring differences in the number of errors made between blocks on the SST, as well as between the three sessions. Exploratory analyses will be labelled as such in the publication of the data**.**

Appendices 4 Task schematics used in study four (chapter five)

Fig 1 Task schematics



Appendices 5 Pre-registration of an exploration of the associations between proactive control, working memory, alcohol sensitivity and overall alcohol use.

Laura Baines Andrew Jones

Introduction

Inhibitory control is defined as the inability to suppress, postpone or alter a response that is no longer necessary or is inappropriate given the current situation (Logan et al, 1984). Numerous laboratory studies have reported associations between inhibitory control and hazardous drinking (Christiansen et al., 2012; Houston et al., 2014), and meta-analyses have demonstrated that inhibitory control is impaired in heavy drinkers/alcohol dependent patients compared to controls (Smith et al, 2014). In particular, exposure to alcohol-related cues is believed to impair inhibition (Jones et al, 2013), and research using alcohol cues embedded into Stop Signal and Go/No-Go tasks has supported this, demonstrating short-term deficits in inhibition (Jones & Field, 2015; Petit et al, 2012).

This evidence however presents an over-simplistic view of inhibitory control as a reactive stopping response, whilst failing to recognise the complexity of the behaviour. A recent cognitive model (Verbruggen et al, 2014) has argued that inhibitory control involves a combination of sequential processes including: signal detection (identifying an inhibitory signal), followed by selecting and executing (or inhibiting) an appropriate action. Additionally, each sub-process is underpinned by other non-inhibitory processes, including proactive control and associative learning, both of which may play a significant role in substance use (Aron, 2011; Verbruggen et al., 2014). By deconstructing inhibition into these separate components we can gain a better understanding of the link between inhibition and alcohol-consumption.

Specifically, some research has suggested that alcohol-cues may induce cognitive biases that effect the maintenance of proactive control and the execution of a reactive stopping response (Stacy & Wiers, 2010). It is possible that these cues compete with inhibitory signals in the environment for attentional selection (Pessoa et al, 2012) reducing the detection of inhibitory signals. Additionally, alcohol-related cues are especially salient for heavy drinkers (Sharma, 2017) which could explain the potential differences in the use of proactive control in heavy and light drinkers. For

example, using a face-word version of a Stroop task (followed by an alcohol or neutral word), Sharma (Sharma, 2017) demonstrated that the performance of the heavy drinkers, but not the light drinkers, was negatively affected by the context of the preceding image. Consequently, light drinkers were thought to be employing proactive control whereas heavy drinkers were using reactive control to complete the task. Nevertheless, it is still not fully understood whether the impairing effects of alcohol cues on inhibitory control arise from effects on proactive control or reactive control (or a combination of these).

Furthermore, event-related potential (ERP) research has demonstrated that alcohol-related stimuli in particular captures the attention of individuals who self – report low sensitivity (LS) to alcohol (e.g. (Bartholow et al, 2010; Fleming & Bartholow, 2014)). In a recent paper by Bailey & Bartholow (Bailey & Bartholow, 2016), it was reported that when LS individuals are faced with task irrelevant alcohol-related stimuli, they experience conflict. When this conflict is infrequent, these individuals can overcome it by using reactive control effectively, however, when this conflict increases, these individuals have difficultly using proactive control efficiently. Therefore, it is possible the individual differences in sensitivity to alcohol may contribute to the effective use of proactive and reactive control.

Importantly, research has also demonstrated that performance in multiple cognitive domains can be predicted by Working Memory Capacity (WMC) (Richmond et al, 2015), which is 'cognitive system responsible for providing access to information required for ongoing cognitive processes' (Wilhem et al, 2013). Indeed, there is some evidence to suggest that individual differences in WMC may account for variance in the ability to implement proactive control (Richmond et al, 2015). This is because WMC is essential to guide future behaviour through the storage of information in an active state (Redick, 2014). Despite this, it is still not fully understood which sub-processes of inhibitory control may be modulated by WMC. Consequently, the aim of this research is to explore the direct and indirect effects of exposure to alcohol cues on overall alcohol use via SSRT, proactive control and WMC. We also aim to investigate whether alcohol sensitivity and WMC are associated with the ability to implement proactive control.

Hypothesis 1: Deficits in proactive control, reactive control, WMC and low alcohol sensitivity will be associated with alcohol use.

Hypothesis 2: There will be a direct association between exposure to alcohol-related cues and overall alcohol use. There will also be an indirect effect of exposure to alcohol-related cues on overall alcohol use via deficits in proactive, reactive control and working memory i.e. Exposure to alcohol-related cues will be associated with deficits in proactive, control reactive control and WMC which in turn will be associated with overall alcohol use.

Hypothesis 3: Alcohol sensitivity will predict the ability to implement proactive and reactive control.

Hypothesis 4: The ability to implement Proactive control will be positively associated with working memory capacity.

Method

Participants

Heavy drinkers (N=116) will be recruited from the university and wider community using social media and advertisements. The number of participants was decided upon using a power calculation to find a medium effect size ($F^2 = .15$) at $\alpha = .05$, and 90% power with five predictors (craving, reactive control, proactive control, working memory, alcohol sensitivity). Heavy drinking will be defined using UK government guidelines: males and females who consume > 14 UK units of alcohol per week (1 UK unit = 8g of pure alcohol (Department of Health, 2008)). Other inclusion criteria will include being aged 18 or over, a fluent English speaker, self-reported motivation to reduce alcohol consumption and access to a laptop/PC/Ipad. Exclusion criteria will include a self-reported current or previous diagnosis of substance use disorder, ADHD or a psychiatric disorder.

Materials

Computer Tasks

Modified Self-ordered pointing task *(SOPT; Petrides & Miller, 1982)).*

Participants will be shown sets of alcohol-related images e.g. pint of beer, glass of wine, rearranged in different positions in each trial. They will be asked to click on a different picture in a different position using the left hand mouse button (or directly on the screen if using a touch screen device) on each trial. Once they have clicked a picture the next trial begins and the pictures are rearranged. They will be asked to try not to click the same picture during that block. In the first block, participants will be

shown 6 pictures (3 x 2 array) followed by an 8-item (4 x 2 array) block, a 10-item (5 x 2 array) block and finally a 12-item (4 x 3 array) block. The number of errors are used to measure WMC.

Fig 1 Schematic of the Self-ordered pointing task

Modified Stop-signal task (Verbruggen et al, 2014)

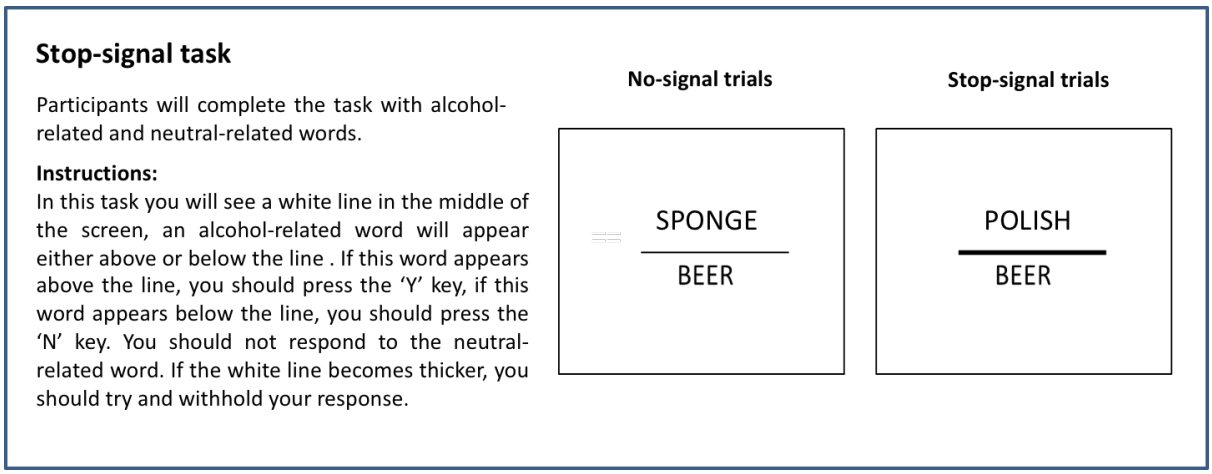
Participants will complete a modified Stop-Signal task, which isolates proactive control and reactive control. On each trial participants will be shown a white line in the middle of the screen and an alcohol-related word e.g. beer will appear either above or below the line. If the word appears above the line, participants should press the 'Y' key, if the word appears below the line, participants should press the 'N' key using the keyboard (these 'keys' will appear at the bottom on the screen on touch screen devices). A neutral word will also be presented but participants should not respond to these. The task will consist of two blocks:

No-signal block: In this block participants will be asked to respond to the alcohol-related word without interruption on 100% of trials.

Signal block: During this block, participants will be asked to respond to the alcohol word without interruption on 75% of trials. On the remaining 25%, the white line will became thicker. Participants will be told to try and withhold their response to the word position if this happens. They will also be given standard stop signal task

instructions that sometimes this will be easy and sometimes this will be difficult or even impossible, but that they should not wait for the line to appear (Verbruggen & Logan, 2009). In the signal block, the delay between the presentation of the alcohol word and the stop signal will be adjusted on a trial-by-trial basis using a tracking procedure (Verbruggen & Logan, 2009). The initial delay will be 250 ms, if participants fail to inhibit the delay will decrease by 50 ms making subsequent inhibition easier, if participants successfully inhibit then the delay will increase by 50 ms making subsequent inhibition more difficult. Proactive control is inferred from the degree of reaction time slowing on stop-signal blocks compared to no-signal blocks (this indicates motivation to inhibit on the stop-signal blocks). Reactive control is inferred from the Stop-signal Reaction Time in the signal block.

Fig 2 Schematic of the modified Stop-signal task



Questionnaires

The Alcohol use disorders identification test (Saunders et al, 1993) will be administered to measure hazardous drinking. This includes 10 fixed-response items and scores are measured between 0 and 40. Higher scores are indicative of greater alcohol consumption, with a score over 8 indicative of hazardous drinking. *The Timeline follow back (Sobell & Sobell, 1990)* will be administered to measure retrospective alcohol consumption in units (one UK unit = 8 g of alcohol), over the previous two weeks. A guide providing the number of units in standard UK drinks will also be provided to assist participants in calculating their alcohol consumption. *The Alcohol Sensitivity* Questionnaire (Fleming et al., 2016) also be administered.

This includes 15 items asking participants how many alcoholic drinks they must typically drink to experience alcohol-related effects. 9 of these items are associated with lower doses of alcohol and stimulation (e.g. increasing talkativeness) and 6 are associated with heavier doses of alcohol and sedation (e.g. passing out). Participants are first asked whether or not they have experienced each alcohol-related effect and if the answer is YES, they are asked to estimate the minimum number of drinks required to experience the lower dose effects or the maximum number of drinks they could consume without experiencing the higher dose effects. High scores on this questionnaire indicate low sensitivity to alcohol. Participants will also be asked when the last time was that they drank alcohol (more than one week ago, within the last week, in the last couple of days, yesterday, today, within the last couple of hours), how they would rate their motivation to reduce alcohol consumption from 0 (not at all) to 10 (extremely) and how they would rate their current urge to drink alcohol from 0 (no urge) to 10 (extreme urge). Lastly, participants will be asked if they were distracted during the computer tasks (Yes/No). We will also include a measure of attention in the AUDIT questionnaire in which participants will be asked to respond with YES.

Procedure/Design

The study will be completed using Inquisit Web 5.0 (Millisecond software). Participants will first be presented with an information sheet and consent form and will be asked to confirm they have read and understood both. Next, they will complete the SST followed by the SOPT. Participants will then give demographic information and complete the questionnaires. Following this, participants will be debriefed and thanked for participation. They will also have the opportunity to input their email address in order to be entered into a prize draw for a £50 amazon voucher.

Proposed analyses

For our dependent variable, we will compute a composite measure of alcohol use to better capture the general pattern of alcohol use, rather than a specific behaviour such as heavy episodic drinking. This is in line with some previous research (e.g. (Baines et al., 2016; Christiansen & Bloor, 2014; Fernie et al., 2013)). This will consist of scores on the AUDIT, units consumed as measured by the TLFB and frequency of heavy episodic drinking (6 + units in a single session for females 8 + for males:

Office of National statistics 2015), z-scored and combined. Stop Signal Reaction time will be calculated using the mean method (Verbruggen et al., 2013). The mean stop-signal delay will be subtracted from the mean go reaction time for the stop-signal block.

Hypothesis 1: Deficits in proactive, reactive control and working memory will predict overall alcohol use. Alcohol sensitivity will also predict overall alcohol use.

We will conduct multiple regression analyses to investigate whether deficits in proactive control, reactive control and working memory predict overall alcohol use. We will also investigate if alcohol sensitivity predicts alcohol use.

Hypothesis 2: There will be a direct association between exposure to alcohol-related cues and overall alcohol use. There will also be an indirect effect of exposure to alcohol-related cues on overall alcohol use via deficits in proactive control, reactive control and WMC i.e. Exposure to alcohol-related cues will be associated with deficits in proactive control, reactive control and WMC which in turn will be associated with overall alcohol use.

We will conduct structural equation modelling in order to assess both the direct and the indirect effects of exposure to alcohol cues on overall alcohol use via SSRT, proactive control and working memory.

Hypothesis 3: Alcohol sensitivity will predict the ability to implement proactive and reactive control.

We will conduct multiple regression analyses to investigate if alcohol sensitivity predicts deficits in proactive and reactive control.

Hypothesis 4: The ability to implement Proactive control will be positively associated with working memory capacity.

We will conduct a simple regression analysis to investigate if WMC is associated with the ability to implement proactive control.

Exploratory analyses

Any exploratory analyses will be labelled as such in the publication of the data**.**

Appendices 6 Pre-registration of the effect of acute stress and alcohol cues on proactive and reactive inhibitory control

Laura Baines Andrew Jones Nicholas Fallon

Research Questions

Research has suggested that impairments in inhibitory control may fluctuate in response to various factors such as alcohol related cues, alcohol intoxication and stress. However, there is limited research focusing on the effect of acute stress on inhibitory control and the research that exists has produced contradictory findings. Furthermore, most of the research has failed to consider the complexity of inhibitory control. A recent cognitive model (Verbruggen, McLaren, & Chambers, 2014) has demonstrated that inhibitory control is not a single process, but rather is made up of sub-components; proactive control (the preparation of a response), signal detection (the identification of the inhibitory signal) and reactive control (the actual stopping of a response). Consequently, this study aims to investigate whether acute stress impairs proactive and reactive control in the presence of alcohol-related cues and whether these deficits relate to individual differences in alcohol consumption.

In addition, two event-related potential (ERP) components; N200 and P300 have been recognised as electrophysiological markers of inhibitory control. However, research investigating the effect of stress on inhibitory control has mainly focused on behavioural inhibition. Therefore, we aim to allow a more specific investigation into the underlying processes behind the effect of stress on sub-processes of inhibitory control and alcohol use using EEG data. Lastly, there is some evidence that individual differences in alcohol-sensitivity (AS) and/or working memory capacity (WMC) may account for differences in the use of proactive and reactive control. However, there is still relatively little known about this. Thus, we also aim to investigate if WMC and AS are associated with deficits in inhibitory control and the magnitude of P300. **Hypothesis 1:** Acute stress will cause deficits in i) proactive slowing, ii) proactive stopping and iii) reactive stopping in the presence of alcohol cues.

Hypothesis 2: Participants will consume more beer (as a % of total fluid) following acute stress compared to the control task.

Hypothesis 3: Following acute stress, impairments in proactive and reactive control will predict unique variance in alcohol consumption.

Hypothesis 4: Acute stress will also lead to differences in the magnitude of P300 and N200 responses in the presence of alcohol cues. The magnitude of these responses to alcohol cues will be associated with individual differences in alcohol consumption.

Hypothesis 5: Alcohol sensitivity will be associated with the ability to implement proactive and reactive control as well as amplitudes of P300 in response to alcohol cues.

Hypothesis 6: Stress will also have an effect on WMC. WM performance will be related to the ability to implement proactive control, P300 responses as well as ad libitum alcohol consumption.

Data collection procedures

Participants will be identified via the University of Liverpool's experiment recruitment scheme but also word of mouth and advertisements placed around campus and social media. We will also submit adverts to the announcement board on the University website.

Inclusion criteria:

1. Are aged 18 years of over
2. Fluent English speaker
3. Are regular alcohol drinkers. Individuals should only participate if they drink at least 14 units of alcohol per week.
4. Provide an alcohol breathalyser reading of 0.0 mg/l. As participants may be given alcohol during the experiment, we will ask them to provide a breathalyser reading before starting the experiment.
5. Like the taste of beer

Exclusion criteria:

1. Have ever received treatment for an alcohol problem, or currently seeking such treatment.

2. Currently taking any medication which may be affected by drinking alcohol (e.g., antidepressants, benzodiazepine), this includes cold and flu medicine, such as paracetamol.
3. Have a current or previous diagnosis of ADHD or a psychiatric disorder
4. Currently suffering from or recovering from any illness that may increase your sensitivity to alcohol, e.g. cold, flu.
5. FEMALES: Breastfeeding or pregnant. As the experiment may involve giving alcohol to drink, if individuals are pregnant or there is any possibility of being pregnant or have had unprotected sexual intercourse since their last period they will NOT be eligible to take part in this study. Participants will be able to self-exempt with out the researcher knowing their sexual history as the exclusion criteria is presented on the information sheet.
6. Have an allergy to beer or fruit juice. Participants will be paid up to £30 of love2shop vouchers or 18 course points. We anticipate data collection to be completed by 1st September 2018.

Sample size

We aim to recruit 40 participants. The number of participants was decided upon using a power calculation to find a medium effect size ($dz = .50$) at $\alpha = .05$, and 90% power. Data collection will be terminated when the stated number of participants are recruited.

Variables

Manipulated variables include condition (within-subjects; stress/control), image in the stop-signal task (alcohol/neutral)

Measured variables include: Ad-libitum alcohol consumption - using a bogus taste-test (Jones et al, 2016) Alcohol sensitivity - inferred from the alcohol sensitivity questionnaire Proactive slowing - inferred from the degree of reaction time slowing on the stop-signal block compared to the no-signal block (this indicates motivation to inhibit on the stop-signal blocks). Proactive stopping - inferred from the proportion of inhibitory failures on the cued stop-signal trials in the signal block (as these involve preparation of responses). Reactive stopping - inferred as the stop signal reaction time in the signal block. Working memory capacity - inferred from the number of errors in the self-ordered pointing task. P300 - inferred from the largest positive peak following

presentation of the stop signal. N200 - inferred from the first negative peak occurring prior to the P300. Fz, Pz, Cz - these are midline electrodes inferred from the EEG.

Indices

SSRT will be calculated using the mean method (Verbruggen, Chambers, & Logan, 2013). The mean stop-signal delay will be subtracted from the mean go reaction time for the signal block separately for each condition. Proactive slowing will be calculated by finding the mean of the reaction times for go only trials in the signal blocks separately for each condition. We then will subtract the mean reaction times for the no-signal block from the go only means. Proactive inhibition will be calculated using the proportion of inhibition failures separately for each condition.

Design plan

This experiment uses a within-subjects design. Participants will complete both a control session and a stress session, the order of which will be counterbalanced.

Analysis plan

Manipulation check: We will run a 2 (condition; control, stress) x 3 time (before manipulation, after manipulation, before debriefing) repeated measures ANOVA in order to check the manipulation of stress has worked.

Hypothesis 1: Deficits in reactive control will be investigated using a 2 (condition; control, stress) x 2 (image; alcohol, neutral) repeated measures ANOVA on SSRTS in the signal block. The same will be conducted on the proportion of inhibition errors in the signal block to investigate proactive stopping. We will also conduct a 2 (condition; control, stress) x 2 (block; no-signal, signal) x 2 (image; alcohol, neutral) repeated measures ANOVA on go reaction times to measure proactive slowing.

Hypothesis 2: A paired samples t-test will be conducted on the beer consumed (as a % of total fluid) in the ad libitum taste test between the stress condition and control condition.

Hypothesis 3: Multiple regressions will be conducted investigating if proactive and reactive control predict unique variance in beer consumed (as % of total fluid) in the ad libitum taste test for each condition (stress, control) separately.

Hypothesis 4: 2 (condition: Stress vs No-Stress) x 2 (image: Alcohol vs Neutral) x 3 (Electrode: Fz, Cz, Pz) repeated measures ANOVAS will be conducted on P300 and N200 mean amplitudes to investigate differences following stress.

Hypothesis 5: Multiple regression analyses will be conducted to investigate if alcohol sensitivity predicts deficits in proactive and reactive control as well as P300 amplitudes separately across conditions.

Hypothesis 6: A paired samples t-test will be conducted on the number of errors made in the self-ordered pointing task between conditions (stress, control). We will then run multiple regression analyses to investigate if working memory capacity is associated with proactive control, P300 magnitudes and beer consumed in the ad libitum taste test. Main effects and interactions will be investigated using the appropriate comparisons. Any other analyses will be labelled as exploratory.

Transformations

Mean reaction times will be subjected to a trimming procedure; reaction times that are less than 200 ms or more than 2000 ms or 3 standard deviations outside of the individual mean will be removed.

Follow-up analyses

Significant main effects and interactions will be investigated using the appropriate comparisons. The nature of interactions will determine the number of comparisons carried out. We will report all comparisons, including those that are non-significant. Lastly, we will make all data openly available when published to allow for replication of comparisons.

Inference Criteria

We will use p is less than .05 criteria for determining if the analyses suggests that the results are significantly different from those expected if the null hypothesis were true. We will use two-tailed tests for each analysis.

Data exclusion

We will examine box-and-whisker plots of our dependent variables and outliers will be removed. We will also disclose if the results are affected when removed.

Missing data

Participants with missing data will be excluded from the analysis.

Fig 1 Task schematic of Stop-Signal task

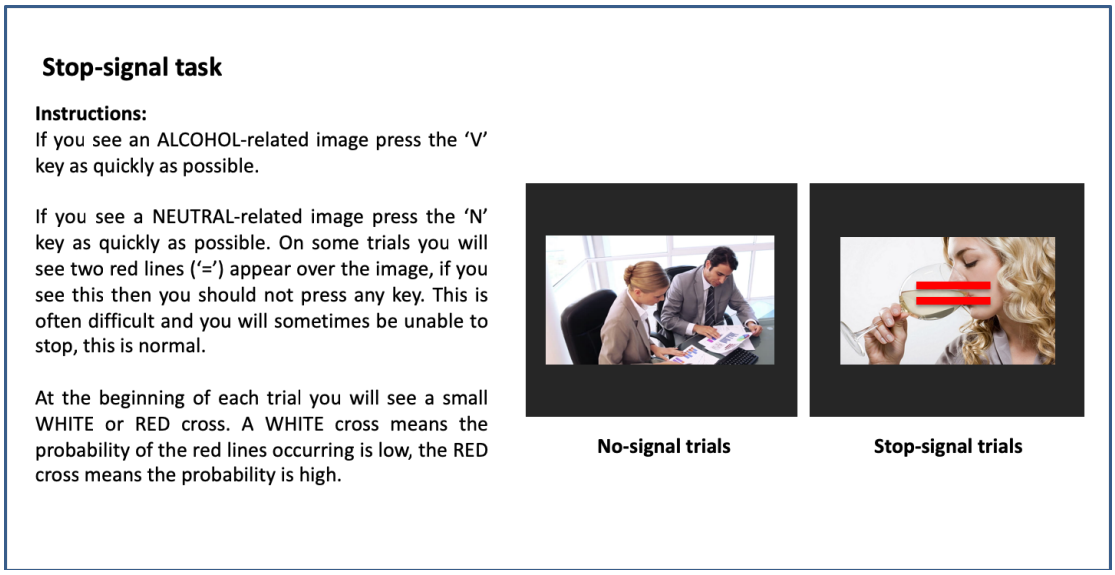


Fig 2 Task schematic of Self-Ordered Pointing task